

EVALUATION OF COGNITIVE DOMAINS
IN PEOPLE WITH PARKINSON'S DISEASE –
A NETWORK APPROACH

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ABSTRACT

Background & Objective: Cognitive impairment is a frequent non-motor symptom in people with Parkinson's disease (PwPD), potentially impacting patients' quality of life and affecting further therapeutic decision. Valid and reliable cognitive diagnostics are thus highly relevant. Cognitive domains are an essential feature of cognitive diagnostics in PwPD, yet they are inconsistently defined by different diagnostic guidelines and lack empirical justification. These issues may lead to unreliable cognitive subtype diagnoses, that is, cognitive profiles based on observed cognitive domain impairments, challenging reliability and validity of cognitive diagnostics. Psychometric network models of cognitive test scores might be a promising alternative for conceptualizing cognitive functioning as a complex, interconnected network. The present thesis project aims to evaluate the concept of cognitive domains in PwPD and to complement it by taking a network perspective on cognitive functioning in PwPD. Specifically, it aims to i) give an overview of existing empirical findings regarding cognitive domains in PwPD, ii) identify the cross-sectional structure of cognitive functioning in empirical data from PwPD, and iii) identify temporal dynamics of cognitive functioning in empirical data from PwPD. Within the empirical analyses, we aim to explore the usefulness of network perspectives on cognitive functioning as an alternative to categorical cognitive domain systems.

Methods: The present thesis project comprises three studies: one scoping review and two empirical analyses. The scoping review (study I) featured a preregistered literature search aiming to identify sources of evidence that applied dimensionality reduction methods to cognitive test data from PwPD. The two empirical studies used data from the DEMPARK/LANDSCAPE study, a completed, observational, prospective multi-center cohort study that initially aimed to characterize the natural course of cognitive decline in PwPD. For study II, we applied exploratory graph analysis (EGA) based on psychometric network analysis to extensive cognitive test data (19 cognitive test scores) of $N = 698$ PwPD with different cognitive statuses to investigate the dimensionality structure of cognitive functioning and compare it to a theoretically assumed cognitive domain structure. In addition, we performed a conceptual replication of our analyses with data from a sample of over 60,000 people with

healthy cognition. For study III, we applied dynamic EGA (dynEGA) to the longitudinal DEMPARK/LANDSCAPE cognitive test data, including data from $N = 355$ PwPD with different cognitive statuses and available repeated, yearly follow-up assessments up to three years after baseline (i.e., four time points of yearly assessments). By this, we investigated dimensions of cognitive test scores that showed similar rates of change over time and compared these dimensions to previous findings of study II and the theoretically assumed domain structure. Further, we applied graphical vector autoregression (GVAR) models to explore the sequential cognitive decline, that is, which longitudinal dimensions predict each other over time.

Results: The scoping review included 22 studies that performed dimensionality reduction methods to cognitive test data from PwPD. Synthesis of findings revealed that most studies employed exploratory approaches. Methods and results of these studies were highly inconsistent and none of the studies reproduced their previously assumed cognitive domain structure. In study II, EGA revealed five dimensions of cognitive test scores that differed from theoretically assumed domains and strong associations between cognitive test scores from the same test paradigms. After reducing redundancy in the data, EGA identified a unidimensional structure of cognitive test scores. Findings were conceptually replicated with data from cognitively healthy people. DynEGA from study III found five longitudinal dimensions that again differed from both the cross-sectional findings of study II and the theoretically assumed domains. GVAR models showed two clusters of longitudinal dimensions and indicated a temporal dissociation between card sorting/cognitive flexibility and visuoconstruction.

Discussion & Conclusion: All three studies revealed a considerable gap between theoretical assumptions about cognitive domain structures and empirical findings in PwPD. Interpretation of existing empirical studies is limited by inadequate choice and high heterogeneity of methods. Results of the empirical studies position network models as a promising alternative conceptualization of cognitive functioning compared to categorical cognitive domain systems, as they might better reflect shared cognitive processes and influences of method-specific variances. Additionally, incorporating information about longitudinal trajectories of cognitive decline might enhance diagnostic and prognostic accuracy of cognitive diagnostics in PwPD. Future research will have to develop new measures and indices of cognitive performance within the network framework to initiate the shift towards a holistic view of cognitive functioning.

STUDIES INCLUDED IN THE CUMULATIVE THESIS

The cumulative thesis comprises three key publications, referred to as study I, study II and study III. Study I is a preregistered scoping review with systematic literature search for identifying existing empirical findings on cognitive domains in people with Parkinson's disease. Study II and study III are based on data from the *Dementia and Parkinson's disease/Langzeitbeobachtung dementieller Symptome und cognitiver Parameter sowie Anwendbarkeit neuer prognostischer Marker bei der Parkinson-Erkrankung* (DEMPARK/LANDSCAPE) study (Balzer-Geldsetzer et al., 2011), a completed, observational, prospective multi-center cohort study with the aim to characterize the natural course of cognitive decline in people with Parkinson's disease. For detailed information on the authors' contributions to the studies included in the cumulative thesis, please refer to the scientific contribution statements at the beginning of each studies' summary in chapter 2 *The present thesis project*. The original publications can be retrieved digitally via the links and QR-Codes provided in the chapter *Original Publications* and are additionally reprinted in the *Appendix*.

STUDY I

Scharfenberg, D., Ophay, A., Lessmann, A., Folkerts, A.-K., Kromke, K., Stahl, J. & Kalbe, E. (2026). Understanding cognitive domains in Parkinson's disease: A scoping review of empirical studies. *Neuropsychology Review*. <https://doi.org/10.1007/s11065-025-09691-5>

STUDY II

Scharfenberg, D., Kalbe, E., Balzer-Geldsetzer, M., Berg, D., Hilker-Roggendorf, R., Kassubek, J., Liepelt-Scarfone, I., Mollenhauer, B., Reetz, K., Riedel, O., Roeske, S., Schulz, J.B, Storch, A., Trenkwalder, C., Witt, K., Wittchen, H.-U., Dodel, R. & Ophay, A. (2025). A network perspective on cognition in individuals with Parkinson's disease. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, 17(1), e70091. <https://doi.org/10.1002/dad2.70091>

STUDY III

Scharfenberg, D., Kalbe, E., Ophey, A., Balzer-Geldsetzer, M., Berg, D., Hilker-Roggendorf, R., Kassubek, J., Liepelt-Scarfone, I., Mollenhauer, B., Reetz, K., Riedel, O., Roeske, S., Schulz, J.B, Storch, A., Trenkwalder, C., Witt, K., Dodel, R. & Deserno, M. (2026). Temporal dynamics of cognitive functioning in people with Parkinson's disease. *npj Parkinson's disease*, 12, 86. <https://doi.org/10.1038/s41531-026-01338-3>

LIST OF ABBREVIATIONS

Abbreviation	Definition
AD	Alzheimer's disease
ADL	Activities of daily living
CERAD+	Consortium to Establish a Registry for Alzheimer's Disease Plus
CFA	Confirmatory factor analysis
CFI	Comparative fit index
crossEGA	Cross-sectional exploratory graph analysis
DEMPARK/LANDSCAPE	Dementia and Parkinson's disease / Langzeitbeobachtung dementieller Symptome und cognitiver Parameter sowie Anwendbarkeit neuer prognostischer Marker bei der Parkinson-Erkrankung
DSH	Dual-syndrome hypothesis of cognitive decline in Parkinson's disease
DSM	Diagnostic and statistical manual
dynEGA	Dynamic exploratory graph analysis
EBIC	Extended Bayesian information criterion
EFA	Exploratory factor analysis
EGA	Exploratory graph analysis
GGM	Gaussian graphical model
GVAR	Graphical vector autoregression
glasso	Graphical lasso
MCI	Mild cognitive impairment
MDS	Movement Disorder Society
MGM	Mixed graphical model
MMSE	Mini Mental State Examination
MoCA	Montreal Cognitive Assessment
NCD	Neurocognitive disorder
PANDA	Parkinson Neuropsychometric Dementia Assessment
PCA	Principal component analysis
PD	Parkinson's disease
PD-D	Parkinson's disease dementia
PD-MCI	Mild cognitive impairment in Parkinson's disease
PD-NC	Normal cognition in Parkinson's disease
PIGD	Motor subtype with postural instability and gait difficulties
PRISMA-ScR	Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Review
PwPD	People with Parkinson's disease

RBD	REM-sleep behaviour disorder
RSMEA	Root squared mean error of approximation
SCD	Subjective cognitive decline
TD	Tremor-dominant motor subtype
TEFI	Total entropy fit index
TMT	Trail making test
UVA	Unique variable analysis

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CHAPTER 1 – INTRODUCTION

1.1. PARKINSON'S DISEASE

Parkinson's disease (PD) is neurodegenerative disease names after James Parkinson who was the first to extensively describe symptoms and trajectory of the disease in "An essay on the shaking palsy" in 1817 (Parkinson, 2002). Today, PD is recognized as the second most prevalent neurodegenerative disease, affecting about 6.1 million people worldwide as estimated in 2015 (Feigin et al., 2017). Notably, PD is considered the neurological disease with the fastest growing prevalence (Feigin et al., 2017). Recent projections estimate that in 2050, 25.2 million people will be living with PD worldwide, with an estimated prevalence of 267 cases in 100,00 people, marking an increase of 55% from 2021 (Su et al., 2025). Thus, PD is highly relevant. In this chapter, I will provide a brief overview about clinical characteristics of PD. As the present thesis project focuses on aspects of cognitive diagnostics in people with PD (PwPD), which are discussed in depth in chapter 1.2. and 1.3., this chapter is not to be considered an exhaustive review of all relevant aspects of PD.

1.1.1. Clinical characteristics

Neurologically, PD is characterised by degeneration of dopaminergic neurons in the substantia nigra and accumulation of α -synuclein proteins in Lewy bodies (Vázquez-Vélez & Zoghbi, 2021). Clinically, it is defined by its motor syndrome, manifesting in bradykinesia (i.e., slowness of initiating or executing spontaneous or voluntary movements), together with rigidity (i.e., resistance to passive movement of the major joints), tremor (i.e., involuntary shaking of body parts), or postural instability (Höglinger & Trenkwalder, 2023). The clinical diagnosis of PD is therefore based mainly on these motor symptoms, requiring the presence of bradykinesia together with either rigidity, a resting tremor, or both (Höglinger & Trenkwalder, 2023; Postuma et al., 2015).

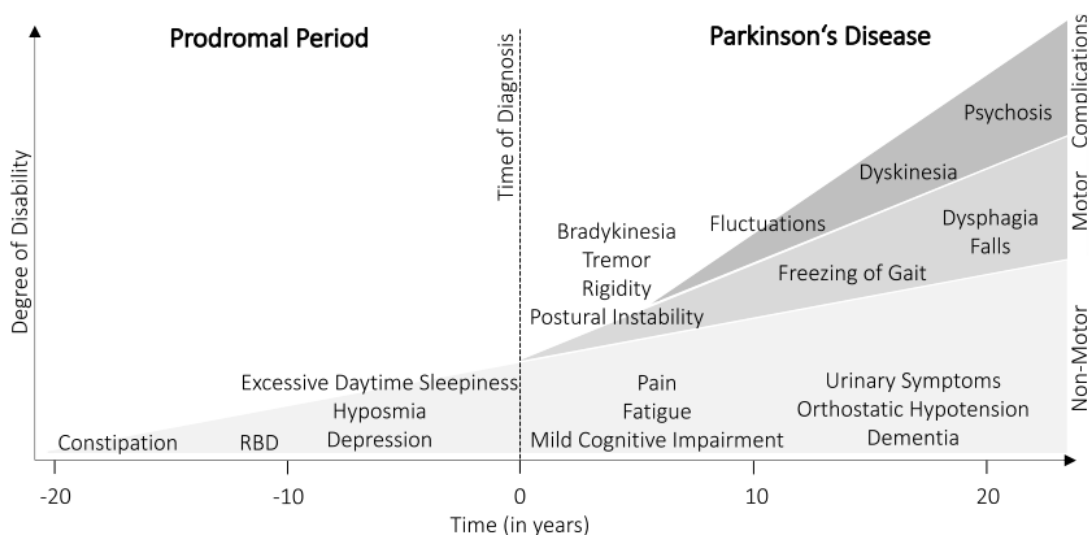
Clinical syndromes of PD can vary, for example showing as different motor subtypes. Widely acknowledged PD motor subtypes include the tremor-dominant (TD) subtype characterized by essential tremor and a subtype with postural instability and gait difficulties (PIGD) characterized by bradykinesia and rigidity (Thenganatt & Jankovic, 2014). Importantly, subtypes have been shown to be associated with different disease trajectories: The TD subtype

is associated with a slow progression and good response to pharmacological treatment, whereas the PIGD subtype is associated with rapid progression and a higher risk for dementia (Thenganatt & Jankovic, 2014). Due to heterogeneous clinical syndromes and disease progression that impact diagnostics based on clinical motor symptoms, the field is currently advancing toward a biological disease definition of PD, highlighting the use of fluid, tissue, and imaging biomarkers for identification of genetic risk, pathological processes, and neurodegeneration before onset of clinical symptoms (Höglinger et al., 2024; Simuni et al., 2024).

Apart from motor symptoms, PD is characterised by various non-motor symptoms that may even occur even before the characteristic PD motor symptoms arise. Early PD non-motor symptoms in this prodromal period before clinical diagnosis can include constipation, REM-sleep behaviour disorder (RBD), excessive daytime sleepiness, hyposmia (i.e., altered smelling sense), and depressive symptoms. Later non-motor symptoms might include pain, fatigue, urinary symptoms, or orthostatic hypotension (Figure 1). Cognitive impairment represents another relevant and frequent cluster of non-motor symptoms and will be discussed in detail in the following subchapter 1.2.2.

Figure 1

Overview of clinical symptoms over time in Parkinson's disease and its prodromal period



Note. RBD = Rapid eye movement sleep behaviour disorder. From *“Effects and mechanisms of working memory training in patients with Parkinson's disease”* (p. 2) by Anja Ophey, 2021, Kölner UniversitätsPublikationsServer (<http://kups.ub.uni-koeln.de/id/eprint/52535>), adapted from Kalia and Lang (2015). Reprinted with permission.

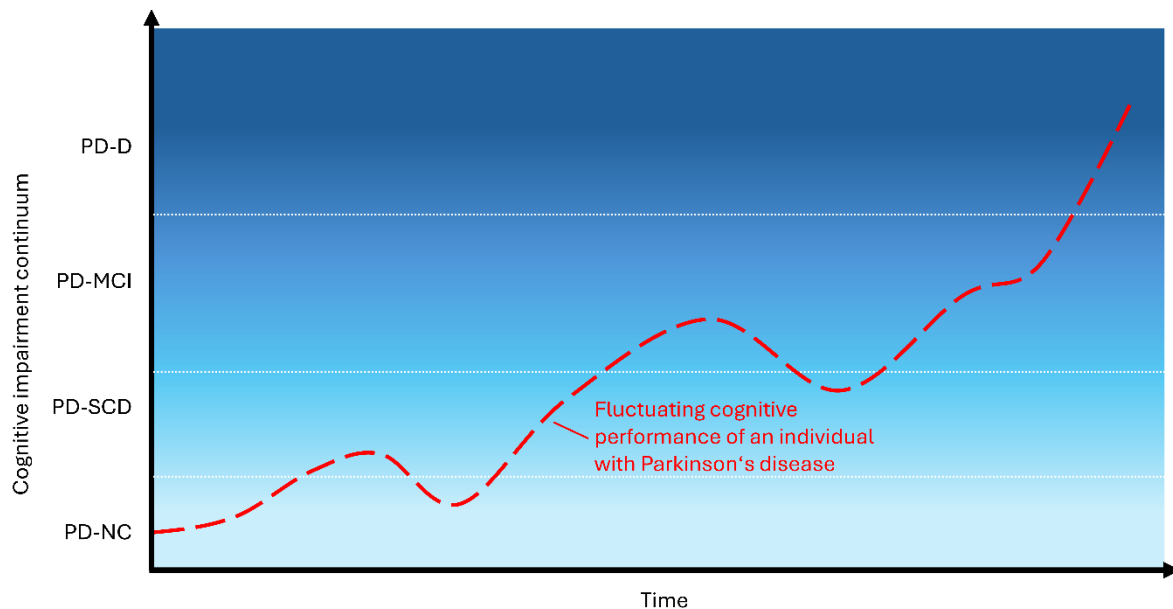
1.1.2. Cognitive impairment

In general, as well as in PwPD, cognitive performance can be viewed as a continuum (see Figure 2) ranging from normal cognition (i.e., norm-adequate cognitive performance), over mild cognitive impairment (MCI) to dementia. MCI is characterized by cognitive performance below the demographically adjusted norm, which, however, does not significantly interfere with activities of daily living (Petersen, 2004). In contrast, dementia constitutes more severe and extensive cognitive impairments that significantly interfere with activities of daily living (American Psychiatric Association, 2013). In addition, subjective cognitive decline (SCD; Jessen et al., 2014), that is, subjective feeling of cognitive decline without objectively detectable cognitive impairment, is increasingly being acknowledged as part of the continuum, often viewed as a risk factor for developing cognitive impairment. Importantly, cognitive performance may fluctuate across the cognitive spectrum, possibly showing (temporarily) remission of cognitive impairment (Aarsland et al., 2021; Koepsell & Monsell, 2012).

In PwPD, the full spectrum of cognitive performance (Figure 2) can be observed (Aarsland et al., 2021). In a sample of $N = 210$ PwPD, one study showed that 18% of participants remained cognitively stable without signs for cognitive impairments over the course of ten years (Bäckström et al., 2022), indicating that some PwPD may remain cognitively unimpaired for several years after diagnosis. However, the results also indicate that the majority of PwPD are at risk for cognitive impairment. Systematic reviews showed relatively high prevalences (up to 36%) of SCD in PwPD (Oedekoven et al., 2022; Siciliano et al., 2024), which has been associated with increased risk for subsequent cognitive decline (Erro et al., 2014; Kim et al., 2026). About 27 % of PwPD present with PD-MCI already at the time of the clinical PD diagnosis (Litvan et al., 2012). A meta-analysis including $N = 7,053$ PwPD from 41 empirical studies concluded that PD-MCI is prevalent in approximately 40% of this population (Baiano et al., 2020). For PD-dementia (PD-D), studies suggest that PwPD have a three- to fivefold increased risk of developing PD-D over the disease course compared with individuals without Parkinson's disease (Domellöf et al., 2015). Specifically, studies show that up to 80% of PwPD will eventually develop PD-D (Aarsland et al., 2003; Gallagher et al., 2024; Hely et al., 2008).

Figure 2

Hypothetical example for fluctuating cognitive performance in an individual with Parkinson's disease



Note. Red dotted line represents the fluctuating cognitive performance of a hypothetical individual with Parkinson's disease across the cognitive impairment continuum over time. White dotted lines represent diagnostic thresholds of cognitive statuses. PD-NC = Parkinson's disease with normal cognition; PD-SCD = Parkinson's disease with subjective cognitive decline; PD-MCI = Parkinson's disease with mild cognitive impairment; PD-D = Parkinson's disease dementia. Adapted from Aarsland et al. (2021) and Oikonomou et al. (2026).

There are several factors that modulate the risk of cognitive impairment in PwPD. Risk factors for cognitive impairment include higher age (Bäckström et al., 2022; Marinus et al., 2018; Uc et al., 2009), lower education (Bäckström et al., 2022; Guo et al., 2019), severity of motor symptoms (Bäckström et al., 2022; Marinus et al., 2018; Uc et al., 2009), or the PIGD subtype (Bäckström et al., 2022; Guo et al., 2019; Uc et al., 2009). In addition, there are several other general influencing factors that modulate risk of dementia, such as depression, physical inactivity, diabetes, or social isolation (Livingston et al., 2024). Importantly, these factors are considered potentially modifiable and it is estimated that about 45% of dementia cases (independent of aetiology) worldwide could be prevented or delayed under optimal conditions (Livingston et al., 2024). These findings correspond to the concept of cognitive reserve, which refers to the ability of the brains ability to adapt cognitive processes and thus to prevent cognitive decline despite facing neural damage (Y. Stern et al., 2020), for example due to

neurodegenerative processes such as degeneration of dopaminergic neurons and the accumulation of α -synuclein in the context of PD. Cognitive reserve is assumed to be a dynamic concept that can be shaped by modifying relevant risk factors, such as education, social activity, healthy and active lifestyle, or cognitive stimulation (Y. Stern et al., 2020). A recent meta-analysis showed that higher cognitive reserve indeed reduces risk of dementia and preserve both cognitive and motor function in patients with α -synucleinopathies, including PD (Saywell et al., 2024).

Consequently, approaches for both prevention of and intervention for cognitive impairment in PwPD have been proposed. Lifestyle intervention (such as more physical activity, healthy diet, reducing stress) are proposed to provide benefits for several clinical aspects of PD, for example, on slowing neurodegeneration, motor symptoms (Trinh et al., 2026), and cognitive decline (Kalbe & Schaeffer, 2026; Kalbe et al., 2025). In addition, cognitive performance in PwPD can be improved or stabilized by cognitive interventions, such as (digital) cognitive trainings (Leung et al., 2015). Future approaches might further increase the efficacy of cognitive interventions by tailoring personalized interventions based on individual symptomatic and cognitive characteristics (Kalbe et al., 2018).

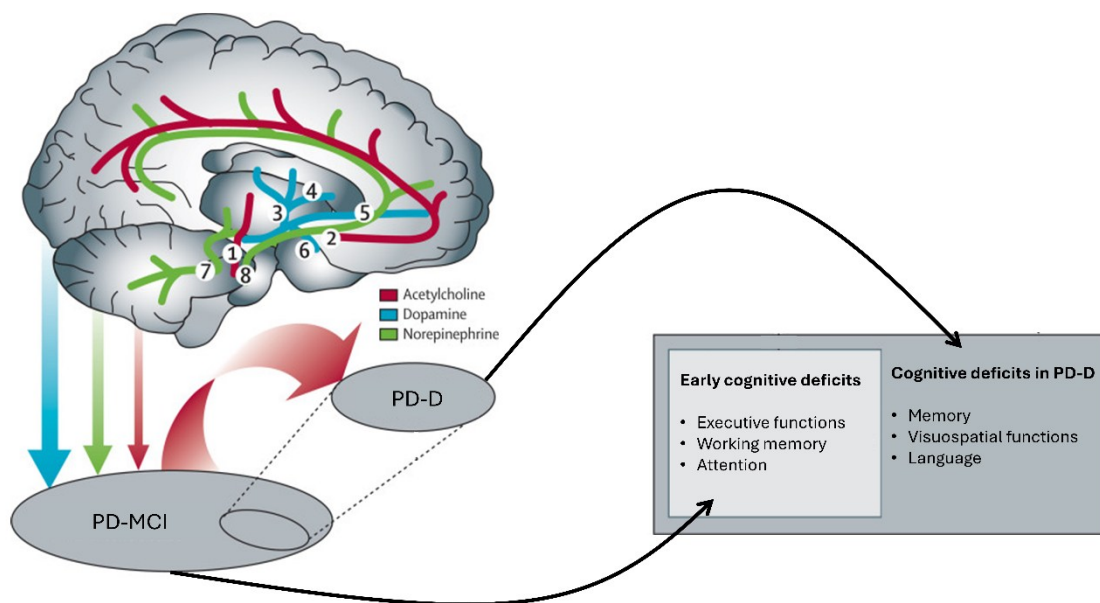
1.1.3. Cognitive characteristics and the dual-syndrome hypothesis of PD

Cognitive impairment in PwPD can affect various cognitive functions, including memory, attention, executive, and visuospatial functions (Aarsland et al., 2010). However, executive dysfunctions have been shown to be the most frequent cognitive symptom of PD-MCI, whereas impairments of memory functions are less common (Kalbe et al., 2016). In addition, impairments of visuospatial abilities appear to be a defining feature of PD (Johnson & Galvin, 2011). Consequently, neuropsychological profiles differ from those of people with Alzheimer's disease (AD), where amnesic MCI (i.e., mild cognitive impairment with impaired memory functions) is the defining neuropsychological characteristic of this clinical group (Ophey et al., 2021). However, the interindividual profiles of cognitive impairment and cognitive decline in PwPD can be heterogenous. The dual-syndrome hypothesis of PD (DSH) offers a means to explain such heterogeneity by assuming two distinct but overlapping pathways of cognitive decline in PwPD (Kehagia et al., 2010, 2013):

Path 1 is characterized by dopamine-modulated fronto-striatal impairment, manifesting as early executive and attention deficits. Path 2 is characterized by cholinergic-modulated posterior and temporal lobe impairments manifesting as dysfunctions in language functions, memory, and visuospatial abilities, and typically shows a later onset but more rapid decline to PD-D.

Figure 3

The dual-syndrome hypothesis of cognitive decline in Parkinson's disease



Note. The dual-syndrome hypothesis explains heterogeneity of cognitive decline in people with Parkinson's disease. PD-D = Parkinson's disease dementia. PD-MCI = Parkinson's disease with mild cognitive impairment. Reprinted and adapted from The Lancet (9), Kehagia, Barker & Robbins, *Neuropsychological and clinical heterogeneity of cognitive impairment and dementia in patients with Parkinson's disease*, p. 1200-1213., Copyright (2010), with permission from Elsevier.

Evidence for the DSH was found in neuroimaging studies investigating the neurobiological basis of cognitive impairment in PD (Hirano, 2020) and in a study that found EEG alterations in PwPD with the fronto-striatal subtype but not in PwPD with the posterior-cortical subtype (Betrouti et al., 2022). Studies investigating the DSH from a cognitive-behavioural perspective have provided partial support. One study reported that PwPD could not be reliably categorized according to the DSH based on their cognitive profile and observed no difference in the risk of developing PD-D for those identified as the fronto-striatal subtype

and those identified as the posterior-cortical subtype (Summers et al., 2024). Another study concluded that the DSH is supported after finding more rapid decline of cognitive performance in various cognitive test scores associated with verbal memory functions, executive functions and visuospatial abilities in PwPD with the posterior-cortical subtype (Pourzinal et al., 2023). However, only few longitudinal studies have examined cognitive performance using an extensive neuropsychological test battery (Roheger et al., 2018), which would be necessary to test the assumptions of the DSH robustly.

In sum, the DSH assumes that distinct neurobiological disease mechanisms manifest in distinct cognitive profiles, which are in turn are linked to different disease trajectories. Other studies – although not explicitly referring to the DSH – also associate specific cognitive profiles with disease progression (e.g., Wood et al., 2016). Therefore, valid and reliable neuropsychological diagnostics for identifying these profiles are of high clinical relevance.

1.2. NEUROPSYCHOLOGICAL DIAGNOSTICS IN PwPD

Neuropsychological diagnostics is concerned with measuring cognitive performance and can serve several purposes: (a) to detect cognitive impairment and determine its severity; (b) to monitor changes in cognitive performance across repeated assessments; and (c) to identify cognitive profiles, that is, map which specific cognitive functions are impaired and which are preserved.

Identifying such cognitive profiles can be essential for a) linking the cognitive profile to a probable underlying disease aetiology to establish a clinical diagnosis (e.g., executive dysfunctions and impaired visuospatial abilities might suggest PD, whereas memory and language impairments could point toward AD), for b) planning individualized cognitive training interventions that target impaired cognitive functions, or for c) associating the cognitive profiles with other variables to identify predictors of disease progression or to infer disease mechanism, as exemplified in the context of the DSH.

1.2.1. Diagnostic criteria for cognitive impairment

Various diagnostic criteria for cognitive impairment exist. They can be disease-specific or generic, applicable when the underlying aetiology for the cognitive impairment is unknown.

Two diagnostic criteria guidelines that are particularly relevant for cognitive diagnostics in PwPD are

1. the diagnostic criteria for neurocognitive disorder (NCD) from the Diagnostic and Statistical Manual (DSM) by the American Psychiatric Association (American Psychiatric Association, 2013), and
2. the diagnostic criteria for PD-MCI (Litvan et al., 2012) and PD-D (Emre et al., 2007) by the Movement Disorder Society (MDS).

Both guidelines share the core features of cognitive diagnostics already described: A diagnosis of mild NCD or PD-MCI requires a moderate cognitive decline, demonstrated by cognitive performance below normative levels in one or more cognitive domains, without significant impact on activities of daily living (ADL). A diagnosis of major NCD or PD-D requires more severe cognitive impairment in one or more cognitive domains that significantly interferes with ADL.

Following the guidelines of the MDS for the diagnosis of PD-MCI, there are two levels of neuropsychological diagnostics (Litvan et al., 2012). Level I diagnostics aim primarily at detecting cognitive impairment; they do not characterize detailed cognitive profiles. Consequently, level I assessments are usually administered at the start of the diagnostic process to decide whether further, more fine-grained evaluation is needed. Level I assessments are time-efficient, brief cognitive screening tests that often yield a single “global cognition” score, which is compared with a defined cut-off score indicating cognitive impairment. For cognitive diagnostics in PwPD, the MDS guidelines recommend to administer screening scales that have been developed specifically for or validated for use in PD, such as the Montreal Cognitive Assessment (MoCA; Dalrymple-Alford et al., 2010; Nasreddine et al., 2005), the Mattis Dementia Rating Scale (Llebaria et al., 2008), the Parkinson’s Disease Cognitive Rating scale (Pagonabarraga et al., 2008), or the Scales for Outcomes of Parkinson's disease – Cognition (Marinus et al., 2003). Additionally, other cognitive screening tests exist that were developed specifically for the use in PwPD, such as the German Parkinson Neuropsychometric Dementia Assessment (PANDA; Kalbe et al., 2008). Other unspecific cognitive screenings – for instance, if the aetiology is (yet) unknown – include the Mini Mental State Examination (MMSE;

Folstein et al., 1975) or the German Dementia-Detection (Kalbe et al., 2004) along with the widely used MoCA.

Level II diagnostics comprise more elaborate neuropsychological test batteries that allow for definition of cognitive profiles and the establishment of differential diagnoses. Level II neuropsychological assessments are usually validated and standardised on normative sample, so that an individual's test score can be compared to age-, gender-, and education-specific norms, yielding standardized scores (e.g., z-score, T-score, percentile). These standardized scores are then interpreted according to established diagnostic criteria for cognitive impairment. Level II neuropsychological test batteries are either available as a fixed set of normed and validated tests – for example, the Consortium to Establish a Registry for Alzheimer's Disease Plus battery (CERAD+; Morris et al., 1989; Schmid et al., 2014) or the Neuropsychological Assessment Battery (R. A. Stern & White, 2003) - or they are compiled ad hoc by clinicians and researchers by assembling single validated cognitive tests. Ideally, a level II neuropsychological test battery contains enough tests to assess a wide spectrum of cognitive functions across cognitive domains. However, diagnostic guidelines differ significantly in their classification of cognitive functions to and their definition of cognition domains. In the following chapter, I will discuss the concept of cognitive domains and their relevance for cognitive diagnostics in PwPD in more detail.

1.3. COGNITIVE DOMAINS

The concept of cognitive domains is central to both DSM and MDS diagnostic criteria for cognitive impairment. The DSM criteria for mild/major NCD require “evidence of [moderate/significant] cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual–motor, or social cognition)” (American Psychiatric Association, 2013). Although the DSM does not explicitly recommend it, it is common practice to further subtype NCD by the number of affected domains (single or multiple domain) or by type (e.g., amnesic or non-amnesic NCD) (e.g., Andrews et al., 2026; Schild et al., 2023).

The PD-MCI diagnostic criteria recommend a level II assessment “that includes two tests within each of the five cognitive domains (i.e., attention and working memory, executive,

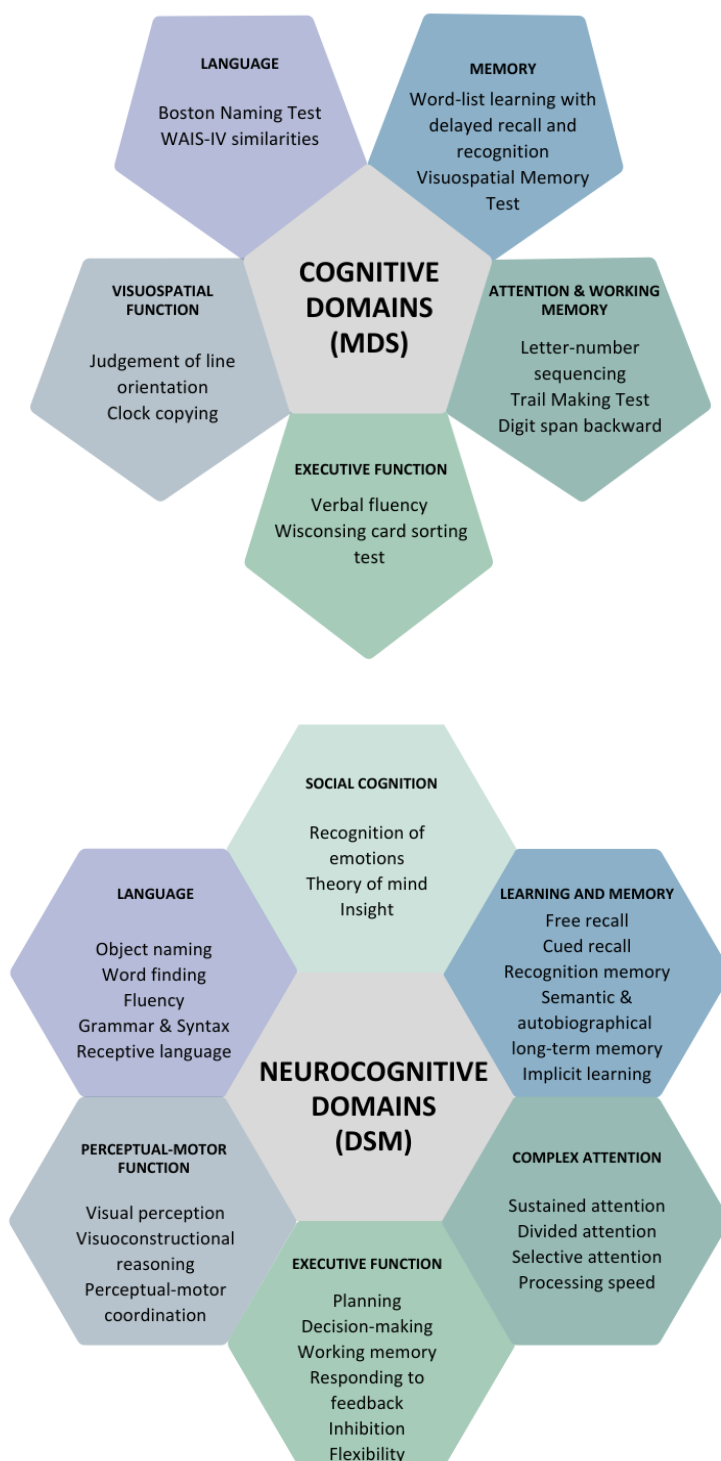
language, memory, and visuospatial)” and requires “impairment on at least two neuropsychological tests, represented by either two impaired tests in one cognitive domain or one impaired test in two different cognitive domains” (Litvan et al., 2012). They explicitly state the option of subtype classification when adequate level II assessments are available: PD-MCI single domain is defined as “abnormalities on two tests within a single cognitive domain (specify the domain), with other domains unimpaired”, whereas PD-MCI multiple domains is defined as “abnormalities on at least one test in two or more cognitive domains (specify the domains)” (Litvan et al., 2012).

The MDS PD-D criteria also rely on the concept of cognitive domain, stating that “impairment in more than one cognitive domain” is one of the core features of a dementia syndrome in PwPD (Emre et al., 2007). They define five “cognitive features” as cognitive domains (attention, executive functions, visuospatial functions, memory, and language) and additionally list four “core domains” (attention, executive functions, visuospatial functions, and free-recall memory). Furthermore, the MDS PD-D criteria include a literature review that identifies six domains: attention, memory, executive function, construction and praxis, visuospatial function, and language (Emre et al., 2007).

From these summaries of diagnostic criteria, it becomes evident that cognitive domains are a universal, crucial concept in neuropsychological diagnostics, yet the various diagnostic criteria define them differently (sometimes even within the same source). The definitions of cognitive domains diverge in the various aspects. One reason for these differences seems to be that both the DSM and the MDS cognitive domain definitions rely solely on expert consensus. Although expert consensus can be a reliable procedure for developing criteria, there is no indication that expert consensus for definitions of cognitive domains are grounded in valid empirical evidence. Below, I will outline the differences between the DSM NCD and the PD-MCI cognitive domain definitions. For simplicity, the MDS PD-D definition is omitted from this comparison because it does not provide a coherent cognitive domains taxonomy (Emre et al., 2007).

One striking difference between the DSM (American Psychiatric Association, 2013) and the MDS (Litvan et al., 2012) cognitive domain definitions is the number of domains: The DSM lists six cognitive domains - including social cognition as a distinct cognitive domain – whereas

the MDS defines five cognitive domains. Apart from this, the two systems use very similar names and constructs, suggesting a comparable underlying cognitive domain structure. A second difference is that the DSM defines cognitive domains abstractly, assigning cognitive functions to domains, whereas the MDS pairs each cognitive domain with specific cognitive tests. In addition, there are slight variations in the naming of domains, such as “learning and memory” in the DSM versus “memory” in the MDS criteria; “perceptual-motor function” in the DSM versus “visuo-spatial function” in the MDS criteria; “complex attention” in the DSM versus “attention and working memory” in the MDS criteria. Although these differences appear minor, they reflect deeper conceptual divergences with potentially significant impact on neuropsychological diagnostics. For instance, the difference between “complex attention” and “attention and working memory” goes beyond just an arbitrary naming issue. As apparent from the name, the MDS places the “digit span backward” task - which is typically viewed as a working memory task – under the attention domain, whereas the DSM assigns working memory to the executive function domain. Likewise – even though not reflected in the cognitive domain names – verbal fluency is classified as a language function in the DSM, while the MDS recommends verbal fluency tasks as measures of executive function. For a visual representation of DSM and MDS domain definitions, see Figure 4.

Figure 4*Cognitive domain definitions*

Note. MDS= Movement Disorder Society diagnostic criteria guidelines for mild cognitive impairment in people with Parkinson's disease (Litvan et al., 2012). DSM = Diagnostic and Statistical Manual guidelines for diagnosing neurocognitive disorder (American Psychiatric Association, 2013).

1.3.1. Clinical relevance of cognitive domain definitions

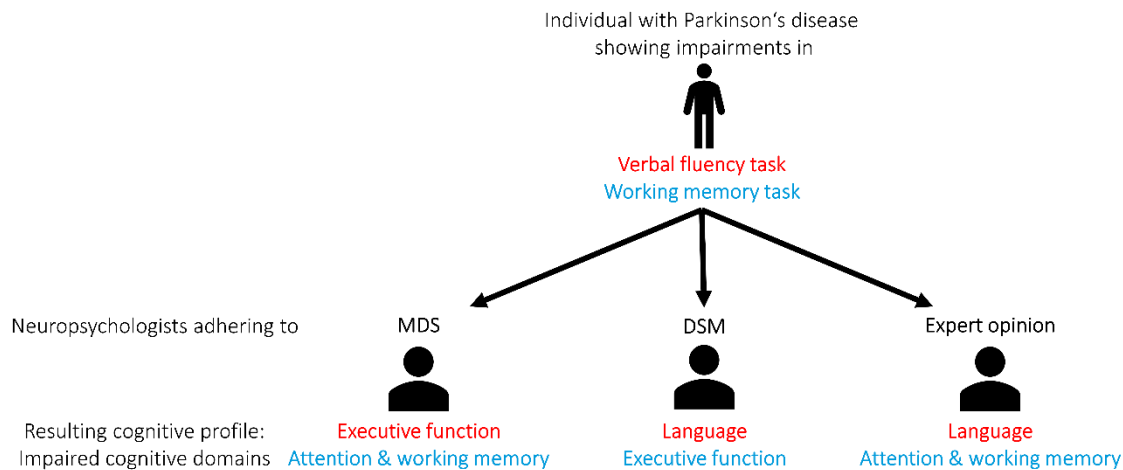
Although the differences in cognitive domain definitions may appear negligible at first glance, they can have substantial impact on clinical diagnoses and subsequent therapy. Consider an individual with PD-MCI who is evaluated by two clinical neuropsychologists using the same extensive level II cognitive test battery. The test battery includes a digit span backwards task (for assessing working memory) and a verbal fluency task, with results of both test scores indicating cognitive impairment. The first neuropsychologist follows the DSM diagnostic criteria for NCD (American Psychiatric Association, 2013), whereas the second clinical neuropsychologist follows the MDS diagnostic criteria for PD-MCI (Litvan et al., 2012). Both neuropsychologists would assign a mild NCD (DSM) or PD-MCI (MDS) diagnosis, but they would describe different cognitive profiles. According to the DSM criteria, the hypothetical individual presents with cognitive impairments in executive function (digit span backwards) and language (verbal fluency). According to the MDS criteria, the same individual presents with cognitive impairments in attention & working memory (digit span backwards) and executive functions (verbal fluency). Notably, a third clinical neuropsychologist might use a different domain mapping based on their own expert opinion – for example, classifying digit span backward as an attention/working memory task and verbal fluency as a language task – resulting in a cognitive profile describing impairments in attention/working memory and language functions. Thus, the choice of domain definition directly influences the reported cognitive profiles (i.e., cognitive subtyping), even when the underlying test results are identical (Figure 5).

The hypothetical scenario described above and in Figure 5 illustrates how parallel domain definitions in clinical practice may affect validity (i.e., we cannot be certain which domains are truly impaired) and reliability (i.e., identical neuropsychological assessments may yield different subtype diagnoses) of cognitive diagnostics. Importantly, no literature has yet examined the prevalence of such varying cognitive subtypes in empirical data from PwPD, although the issue of varying subtypes depending on diagnostic guidelines criteria have been mentioned in the context of the introduction of the PD-MCI MDS guidelines that may have led to epidemiological shifts in the prevalence of single- versus multiple-domain subtypes (Goldman et al., 2018). Supporting the claim of potentially unstable cognitive subtypes, one

study found that the cognitive subtypes identified according to the DSM guidelines were unstable in a Korean sample of people with MCI (Han et al., 2012).

Figure 5

Clinical relevance of inconsistent cognitive domain definitions



Note. Guidelines for cognitive diagnostics propose different cognitive domain definitions. Inconsistent cognitive domain definitions may lead to unreliable cognitive subtype diagnoses in clinical practice. MDS = diagnostic criteria for mild cognitive impairment in Parkinson's disease by the Movement Disorder Society. DSM = diagnostic guidelines for neurocognitive disorder in the Diagnostic and Statistical Manual.

However, this issue has fundamental implications for both research on cognitive impairment in PwPD and for the individuals being diagnosed. As noted earlier, cognitive subtypes (or profiles) are frequently used as predictors for disease progression (e.g., Wood et al., 2016). If subtype classifications are invalid and unreliable, research findings might become inconsistent. The limited support for the DSH in neuropsychological studies, contrasted with clearer results from neuroimaging and EEG studies, may reflect problems of cognitive domain definitions. In clinical practice, different cognitive subtypes may dictate therapeutic decisions, such as the design of personalized cognitive training interventions in PwPD (Kalbe et al., 2018). If cognitive subtypes are inaccurately identified, personalized interventions cannot achieve their full potential to improve or stabilize cognitive performance.

1.3.2. Empirical evidence for cognitive domains

Instead of relying on expert consensus, cognitive domain definitions should be grounded in empirical data to improve validity and reliability. Although cognitive domains are

latent construct that cannot be measured directly, empirical analyses might reveal their underlying structure. Theoretically, cognitive functions grouped within cognitive domains are often presumed to share a common neurobiological basis. For instance, brain regions have been identified to be primarily associated with language functions (e.g., Ardila et al., 2016), executive functions (e.g., Carpenter et al., 2000) or memory (e.g., Rolls, 2000). On a functional-behavioural level, performance of cognitive tasks categorized within the same cognitive domain should be positively correlated beyond the general positive manifold usually observed across all cognitive abilities (van der Maas et al., 2006). Consequently, it should be possible to identify clusters of correlated cognitive tests in neuropsychological data which could be interpreted as cognitive domains. These clusters are typically extracted by dimensionality reduction methods such as factor analysis (e.g., Dowling et al., 2010; Park et al., 2012) or principal component analysis (PCA; e.g., Lambert et al., 2018).

There are only few studies that have applied dimensionality reduction methods to cognitive test data from PwPD. Liepelt-Scarfone et al. (2012) applied exploratory factor analysis (EFA) on comprehensive cognitive test data from $N = 121$ PwPD with varying cognitive statuses. Using a combination of the Kaiser-Guttman criterion, scree-plot inspection, and oblique rotation, they extracted six factors interpreted as cognitive domains *frontal-lobe function*, *word-list memory and recall*, *attention*, *logical memory*, *praxis and visual perception*, and *fluency and naming ability*. Cholerton et al. (2014) applied PCA to cognitive test data from $N = 96$ PwPD with PD-MCI. After applying the Kaiser-Guttman criterion and varimax orthogonal rotation, they identified seven components labelled *attention/processing speed*, *fluency/visuospatial*, *contextual declarative memory*, *working memory/executive*, *list-learning declarative memory*, *construction*, and *language*. These two examples illustrate the heterogeneity of methodological choices (statistical technique, rotation methods, sample characteristics) and of the resulting cognitive domain labels. Importantly, neither set of identified “cognitive domains” aligns with the DSM or MDS cognitive domain definitions. To date, no systematic overview has synthesized such findings from dimensionality reduction methods applied to cognitive test data from PwPD to evaluate support for existing cognitive domain frameworks or to propose an empirically derived cognitive domain structure.

1.3.3. Assumption of temporal stability

One implicit assumption of the cognitive domain concept is temporal stability. Neither the DSM nor the MDS criteria notes that the proposed cognitive domain structure might change, nor do they justify why it should remain fixed. For both diagnostic guidelines, the cognitive domain definitions are essentially identical for earlier (mild NCD/PD-MCI) and more severe (major NCD/PD-D) stages of cognitive impairment, implying that the same set of cognitive test scores forms a given cognitive domain both cross-sectionally and longitudinally. Consequently, we would expect cross-sectional correlations among cognitive test scores to remain stable over the course of aging or further cognitive decline, so that cognitive test scores within an empirical cluster change at a similar rate and in the same direction. Even if this holds true, different cognitive domains could evolve disparately, resulting in disease-specific (e.g., focus on executive, attention, and visual-spatial impairment in PwPD versus focus on memory and language impairment in people with AD, as described in chapter 1.1.3.) or subtype-specific cognitive profiles (e.g., earlier executive dysfunction versus later attention impairment with more rapid decline according to the DSH; Kehagia et al., 2010, 2013).

However, most cognitive tests tap multiple cognitive functions, often times also across various cognitive domains (Steyvers & Schafer, 2020), for example memory, attention, and language functions in verbal memory tasks. Therefore, a single cognitive test score may reflect simultaneous decline in one domain and compensation from another, meaning that longitudinal change rates can differ across cognitive tests within the same domain. As a result, cognitive domain clusters derived from longitudinal data may not match those obtained from cross-sectional data. These systematic shifts in the structure of cognitive functioning must be taken into account when interpreting neuropsychological diagnostics.

To conclude, cognitive domains are an essential concept in neuropsychological diagnostics, yet they remain ill-defined and lack empirical grounding. Existing empirical evidence on the cognitive domain structure in PwPD is heterogenous with varying statistical methods and sample characteristics which likely explains the absence of a systematic overview on this matter. Applying cognitive domains strictly as categorical entities while ignoring interrelations among cognitive functions and test scores undermines the validity and reliability of cognitive (subtype) diagnoses.

1.4. THE NETWORK APPROACH IN NEUROPSYCHOLOGY

Network models can provide a holistic view of interrelated cognitive functions, offering a promising alternative approach to categorical cognitive domain systems. Modelling cognition as network models is termed *network neuropsychology* (Ferguson, 2022). A *network model* is a statistical or graphical representation of these interrelations, typically visualizing empirical correlations among neuropsychological test scores derived from *psychometric network analysis* (although network model as a general term can also represent abstract and theoretical representations of latent cognitive functions). In the network neuropsychology framework, *nodes* represent neuropsychological test scores and *edges* indicate associations between pairs of nodes; the interpretation of edges varies with the specific analysis method. The following chapter reviews psychometric network analysis methods, their interpretation in neuropsychological research, and discusses the strengths and limitations of applying network models to cognitive test data.

1.4.1. Psychometric network analysis

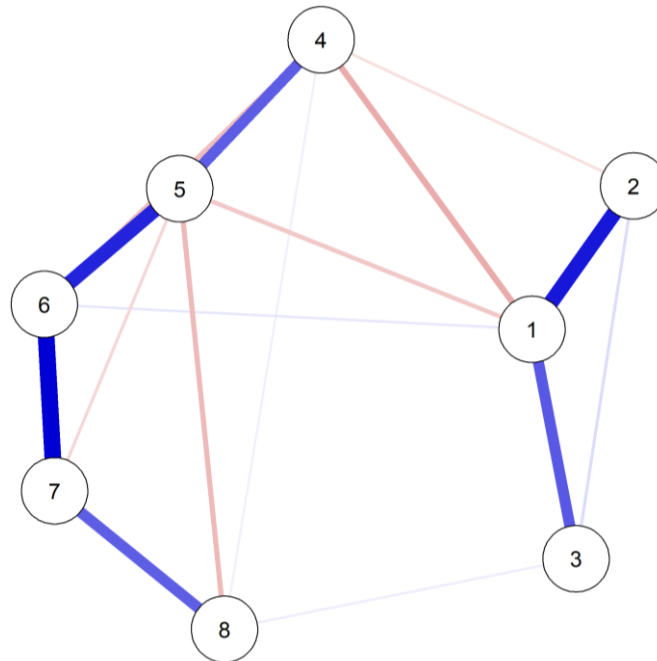
The development of psychometric network analysis has been closely tied to the development of network models in clinical psychology and psychopathology (Borsboom & Cramer, 2013; McNally, 2021), which arise from the network theory of mental disorders (Borsboom, 2017). This subchapter provides an overview of relevant psychometric network analysis methods (Borsboom et al., 2021) and links them to neuropsychological research questions. This overview is not intended to be an exhaustive catalogue of network analysis methods but focuses on network analysis methods relevant for the present thesis project (cross-sectional network analysis, longitudinal network analysis with panel data, and exploratory graph analysis).

Cross-sectional network analysis

Cross-sectional psychometric network analysis requires a large, independent sample measured at a single time point. In neuropsychology, such data could be the baseline assessment of a large cohort study that administered an extensive neuropsychological test battery to PwPD. The data may be binary (e.g., impaired versus unimpaired on a cognitive test), continuous (e.g., standardized neuropsychological test scores such as z-scores or T-scores),

ordinal (e.g., Likert-like response scales), or a mix of these types. Statistical methods exist for various data modalities: Binary data require Ising models (van Borkulo et al., 2014), continuous data require gaussian graphical models (GGM, Epskamp, Borsboom, & Fried, 2018), and ordinal or mixed data (i.e., combinations of binary, ordinal, or continuous data) require mixed graphical models (MGM, Haslbeck & Waldorp, 2020). A cross-sectional network model displays conditional associations driven by between-person differences. In a GGM, an edge represents the partial correlation between two variables, controlling for all other nodes within the network model. Edge weights naturally vary because of measurement error; thus, a non-zero partial correlation does not automatically indicate a substantively meaningful link. To prevent overfitting, researchers can choose to employ edge-selection procedures. Edge selection can be executed by a) regularization estimation procedures, introducing a penalty that shrinks small partial correlations toward zero with the optimal penalty being chosen via a model-selection criterion; b) null hypothesis testing, testing each edge for statistical significance, optionally applying corrections for multiple comparisons (e.g., Bonferroni); and c) cross-validation, optimizing the network for out-of-sample predictive performance, for example, using k-fold cross-validation (Borsboom et al., 2021). For continuous data – typical in network neuropsychology – the *EBICglasso* (Epskamp, Borsboom, & Fried, 2018) is the prevailing regularization method for cognitive test score GGMs. It selects the optimal penalty for the graphical lasso (glasso, Friedman et al., 2008) by minimizing the extended Bayesian information criterion (EBIC, Chen & Chen, 2008).

Figure 6 shows an exemplar GGM with eight simulated variables. Typically, green or blue edges denote positive associations, whereas red edges represent negative associations. Thicker edges indicate stronger relationships. In such visualizations, the nodes can either be arranged either circularly or using a *force-embedded layout* such as the Fruchterman-Reingold algorithm (Fruchterman & Reingold, 1991), which places more strongly connected nodes closer together, resulting in an intuitively interpretable layout (Venturini et al., 2021).

Figure 6*Exemplar gaussian graphical model of eight simulated variables*

Note. Blue edges indicate positive pairwise conditional associations; red edges indicate negative conditional associations.

Longitudinal network analysis with panel data

Longitudinal network analysis uses continuous panel data, that is, data from a relatively large sample measured at multiple time points. In neuropsychology, such data could come from a longitudinal cohort of PwPD assessed with an extensive neuropsychological test battery. Various statistical approaches model how variables predict each other over time within the network framework (Freichel, 2023). One approach is panel graphical vector autoregression (GVAR, Epskamp, 2020), which requires at least three time points of assessments and assumes stationarity of the included variables, that is, that statistical properties remain stable over time (Epskamp, 2020).

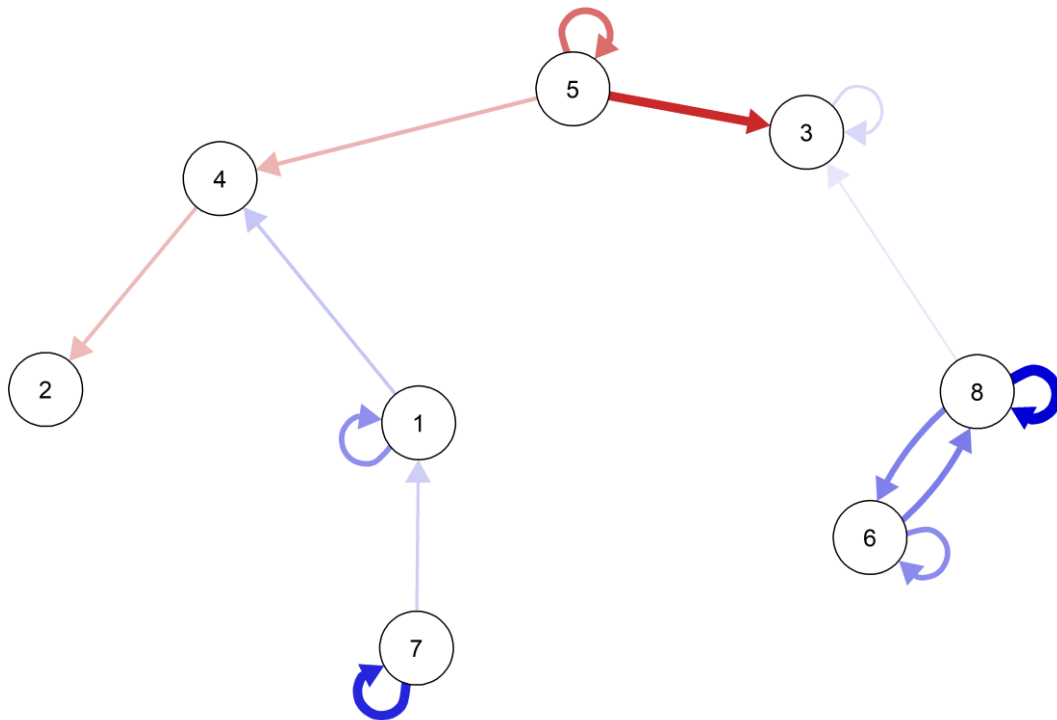
Notably, panel GVAR models can separate within-person from between-person effects and can yield three distinct network models with different interpretations. One model represents average within-person temporal effects (i.e., effects over time), another model

represents contemporaneous effects (i.e., associations within the same time point), and a third model represents between-subject effects.

In the within-subject temporal effects model, each variable is predicted by its own previous values and the lagged values of all other variables, producing autoregressive and cross-lagged estimates (Freichel, 2023). Figure 7 illustrates an example of such a within-subject temporal network model. A directed, positive (negative) edge indicates that a variable at time point t positively (negatively) predicts another variable at time $t+1$. For example, higher performance measured in variable 1 at one occasion predicts higher performance of variable 4 at the next occasion. A directed negative association indicates that high performance in variable 5 at one occasion predicts lower performance of variable 3 at the next occasion. An autoregressive edge refers to the same variable: performance on variable 8 at time t predicts performance on variable 8 at time $t+1$.

Figure 7

Exemplar of a within-subject effect temporal model of eight simulated variables



Note. Blue edges indicate positive directed associations; red edges indicate negative directed associations.

A second network model captures within-subject contemporaneous effects. In this GGM, the undirected edges indicate that two variables co-vary within the same measurement

occasion after accounting for temporal influences, thus reflecting intra-individual covariance (Epskamp, 2020).

The third network model depicts between-subject effects. In this GGM, the undirected edges indicate that individual mean scores on two variables are associated, after accounting for temporal information (Epskamp, 2020). A positive edge thus indicates that people with low performance on one variable tend to also show lower performance on the other variable across time points of assessment.

Exploratory graph analysis

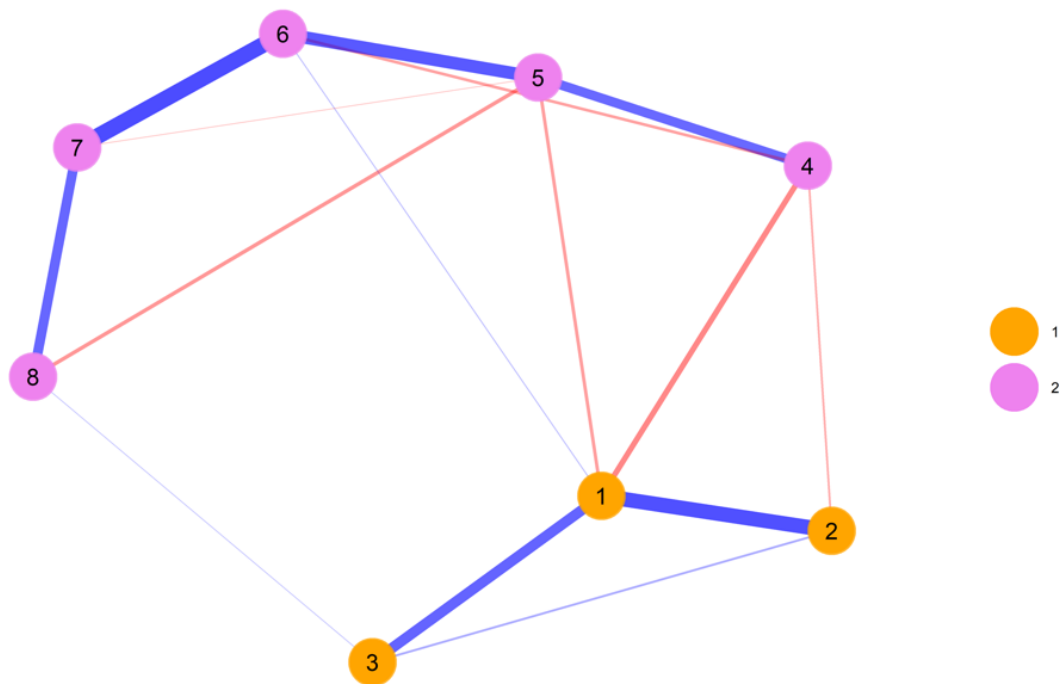
Exploratory graph analysis (EGA, Golino & Demetriou, 2017; Golino & Epskamp, 2017) is a network-based dimensionality reduction method that identifies clusters of variables (dimensions) emerging in empirical network models. Unlike factor analysis, it does not assume latent factors underlying these dimensions. After estimating a network model (e.g., a GGM with the EBICglasso), community detection algorithms such as the Louvain, walktrap, or Leiden algorithms can be applied to extract dimensions (Golino & Christensen, 2025). Model fit of EGA solutions can be compared across algorithms or with alternative techniques using fit indices such as the comparative fit index (CFI), χ^2 , the root mean square error of approximation (RSMEA, Byrne, 1994), or the total entropy fit index (TEFI; Golino et al., 2021) that was specifically developed for EGA. In addition, bootstrapping provides stability assessment of EGA results (Epskamp, Borsboom, & Fried, 2018). Analogous to factor loadings in factor analyses, EGA yields *network loadings* (Christensen & Golino, 2021b) that reflect each node's (unique) contribution to its identified dimension (Christensen et al., 2020). Simulation studies show that EGA performs as well as or better than standard dimensionality reduction methods such as EFA or parallel analysis (Golino & Demetriou, 2017; Golino et al., 2020).

EGA can be applied to both cross-sectional and longitudinal panel data. When applied to longitudinal data – coined *dynamic EGA* (dynEGA; Golino et al., 2022) – it first employs a time-delay embedding approach that estimates the temporal derivatives for each variable and then applies the EGA to the transformed data. DynEGA therefore identifies clusters of variables that change together over time, that is, dynamic latent dimensions (Golino et al., 2022).

In the example below (Figure 8), (dynamic) EGA has been applied to simulated data set of cognitive test scores. For a cross-sectional EGA (crossEGA), edge interpretation is identical to that of the GGMs described earlier. Node color denotes the dimensions to which each variable was assigned by EGA. For a dynamic EGA of longitudinal data, edges represent dynamic associations: A positive edge (e.g., between variables 1 and 2) indicates that the two test scores change at similar rates across measurement occasions, whereas a negative indicates that the two variables change in opposite directions over time.

Figure 8

Exemplar of exploratory graph analysis applied to a gaussian graphical model of eight simulated variables



Note. Blue edges indicate positive pairwise conditional associations; red edges indicate negative conditional associations. Node colors indicate assignment to dimensions empirically derived by EGA.

1.4.2. Network neuropsychology

In network neuropsychology — that is, the application of psychometric network analysis methods to neuropsychological data — network models represent the presence, absence, or strength of associations between cognitive test scores (Ferguson, 2022). Statistically, edges

indicate the association between two test scores after controlling for all other variables in the model. Theoretically, edges are often interpreted as reflecting shared underlying cognitive processes. For example, scores on the Trail-Making Test (TMT, Reitan, 1992) and the d2-test (Brickenkamp & Zillmer, 1998) are expected to be associated because both require selective attention. Similarly, scores on the Stroop interference task (Golden, 1976) are expected to be associated with digit span backwards scores (Härting et al., 2000) because both tasks require executive functions. This reasoning parallels the rationale for using dimensionality reduction methods to define cognitive domains (see chapter 1.3.2.). Another theoretical perspective is the mutualism hypothesis of intelligence (van der Maas et al., 2006), a concept related to cognitive functioning. The hypothesis posits that positive reciprocal associations among cognitive processes foster mutual beneficial development of cognitive functions. The hypothesis can thus be seen as a psychological network model for cognitive development and intelligence (van der Maas et al., 2017). In network neuropsychology, associations between cognitive test scores may indicate reciprocal interactions among underlying cognitive functions, with implications for concepts such as cognitive rearrangement (Ferguson, 2022).

Methodological Considerations in Network Neuropsychology

Several methodological considerations must be taken into account when applying psychometric network analysis to neuropsychological data.

First, there is a considerable lack of dedicated network neuropsychology theory. Although theories of related concepts exist – for example, the mutualism hypothesis of intelligence (van der Maas et al., 2017) or the network theory of mental disorders (Borsboom, 2017) – no formal theory currently guides network neuropsychology. This raises the risk of using network analysis without a clear research aim, producing purely descriptive models that do not address clinically relevant questions in neuropsychology (Fried, 2020).

Second, network neuropsychology has to consider the issue of distinguishing cognitive test scores from underlying cognitive functions (Ferguson, 2022). While a cognitive test score is often assumed and proclaimed to measure a single cognitive function or domain (e.g., the TMT as a measure for attention and working memory; Litvan et al., 2012), most tasks involve multiple interacting cognitive processes and are influenced by mutual task features (Steyvers & Schafer, 2020). Consequently, an edge between two cognitive test scores does not

necessarily reflect a direct link between the presumed underlying cognitive functions. Any inference that goes beyond the observed scores to the level of cognitive processes should explicitly acknowledge this limitation.

Third, the interpretation of a network model is constrained by the variables it contains. Ideally, the selected variables should span an extensive level II neuropsychological test battery so that the network model can approximate the full spectrum of cognitive functioning. However, highly overlapping tests should be excluded to avoid redundancy (Christensen et al., 2023). A further decision concerns whether to include demographic (e.g., age, gender, education), clinical (e.g., depressive scores, disease-specific clinical rating scales), or global cognition measures (e.g., cognitive screening test scores) as nodes. Existing studies show mixed practices – some studies include such variables (e.g., Ferguson, 2021; Grunden & Phillips, 2024b; Tosi et al., 2020), whereas others do not (Nevado et al., 2022; Tosi et al., 2024; Wright et al., 2026). Ultimately, node selection must be driven by the specific research questions and the study's context. Consequently, different studies often use distinct sets of neuropsychological and additional variables, complicating cross-study comparisons (Ferguson, 2022).

Fourth, cross-sectional network models capture only between-person differences and cannot describe within-subject effects. Therefore, inter-individual associations derived from cross-sectional network models do not necessarily translate to intra-individual processes (Borsboom et al., 2021).

Possible applications & existing empirical evidence

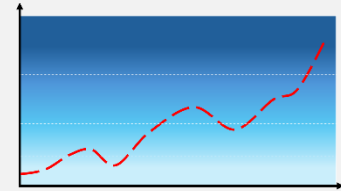
Although applying network analysis methods to neuropsychological data pose challenges, it offers promising opportunities to advance our understanding of cognitive functioning and neuropsychological measurement. By its multivariate analysis of multiple neuropsychological variables and the possibility to visualize them as a graphical network model, network neuropsychology provides a holistic view of inter-test relationships. Because edges are based on partial correlations (Epskamp, Borsboom, & Fried, 2018), they control for all other variables, eliminating bias from potential mediating effects. Hence, network models may inform researchers and clinicians more precisely about how cognitive test scores relate to each other than traditional bivariate, unconditioned correlations.

By offering a holistic view of cognitive functioning, network analyses are a promising alternative to categorical systems such as the concept of cognitive domains. At the same time, network models are not fundamentally opposed to the concept of cognitive domains. In fact, by combining network models with dimensionality reduction methods, such as the exploratory graph analysis (Golino & Demetriou, 2017; Golino & Epskamp, 2017), network models can contribute empirical evidence for clustering of cognitive test scores, that is, cognitive domains.

In addition, longitudinal network analysis of cognitive test scores can provide valuable insights into the temporal dynamics of cognitive functioning, as measured by cognitive test performance. Specifically, dynamic EGA (Golino et al., 2022) is a promising tool for evaluating the concept of temporally stable cognitive domains. Additionally, panel GVAR models (Epskamp, Borsboom, & Fried, 2018) applied to longitudinal neuropsychological data allow separating within-subject effects from between-subject effects, offering insights into intra-individual processes of cognitive functioning.

1.5. INTRODUCTION SHORT SUMMARY

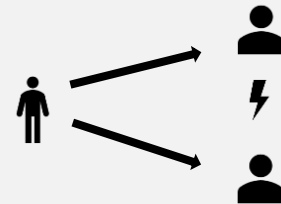
Cognitive impairment is a frequent non-motor symptom in people with PwPD, which may impact patients' quality of life. Hence, **valid and reliable cognitive diagnostics** are highly relevant for this group.



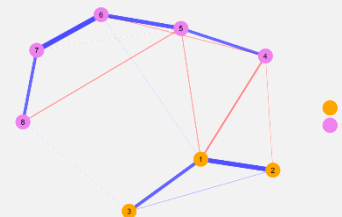
Cognitive domains are an essential feature of cognitive diagnostics in PwPD, yet they are **inconsistently defined** by different diagnostic guidelines, definitions **lack empirical justification**, and **do not take into account potential temporal dynamics**.



These characteristics may lead to **unreliable cognitive subtype diagnoses**, that is, cognitive profiles based on observed cognitive domain impairments, **challenging reliability and validity of cognitive diagnostics**.



Network models of cognitive functioning may be a promising alternative to categorical cognitive domains.



CHAPTER 2 – THE PRESENT THESIS PROJECT

2.1. AIM OF THE PRESENT THESIS PROJECT

The present thesis project aims to evaluate the concept of cognitive domains in PD, which is to date mainly based on expert consensus, empirically and through a network perspective. The thesis' findings should contribute to forming an empirically-based judgement about the validity and reliability of cognitive diagnoses based on cognitive domains in PwPD. Further, it aims to explore the usefulness of applying psychometric network analysis to cognitive test data in neurodegenerative populations such as PwPD.

The studies included in this thesis directly contribute to the overarching research aim of the present thesis. First, study I aims to provide an overview of existing empirical findings on cognitive domain structures in PwPD to evaluate the consistency of empirical findings and their association with cognitive domain-based diagnostic guidelines. Second, study II aims to identify the cross-sectional empirical dimensionality structure of cognitive test scores in a large sample of PwPD and compare the resulting empirical structure with a theoretically assumed structure of cognitive domains. Third, study III aims to identify the longitudinal empirical dimensionality structure in a sample of PwPD and compare the resulting structure to both a theoretically assumed structure of cognitive domains and the cross-sectional empirical structure of study II to test the implicit assumption that cognitive domains are temporally stable. In addition, it aims to identify temporal dynamics of empirical cognitive dimensions to improve our understanding of cognitive functioning and decline mechanisms in PwPD.

2.2. RESEARCH QUESTIONS

- (I) What empirical evaluations of cognitive domain structures exist so far and how consistent are they with diagnostic guidelines based on theoretical assumptions and expert consensus?
 - a) Which methods have been used to empirically evaluate differentiations of cognitive domains and their assigned cognitive tests in PwPD?
 - b) If studies categorized cognitive tests into cognitive domains on a theoretical basis, were they able to reproduce this categorization in their analyses?
 - c) Did studies refer to the DSM definition of cognitive domains or the MDS criteria on diagnosing PD-MCI?

- (II) What is the empirical dimensionality structure of cross-sectional cognitive test scores in a sample of PwPD and how does it differ from a theoretically assumed cognitive domain structure?
- (III) Are cognitive domain structures temporally stable in PwPD?
 - a) What is the empirical dimensionality structure of longitudinal cognitive test scores in a sample of PwPD and how does it differ from a theoretically assumed cognitive domain structure and the empirical dimensionality structure of study II?
 - b) How are longitudinal cognitive dimensions coupled, that is, which dimensions predict each other longitudinally?

2.3. DATA BASE FOR STUDY II AND III – THE DEMPARK/LANDSCAPE STUDY

The data used in study II and III comes from the DEMPARK/LANDSCAPE study (Balzer-Geldsetzer et al., 2011), a completed, observational, prospective multi-center cohort study with the aim to characterize the natural course of cognitive decline in PwPD.

2.3.1. Study design & participants

The DEMPARK/LANDSCAPE study is an observational, prospective cohort study (Balzer-Geldsetzer et al., 2011). Patients were followed up in 12-month intervals for a total of six years, resulting in a maximum of seven assessment points, including baseline assessment. The DEMPARK/LANDSCAPE study collected data from PwPD starting from November 2009. Participants were recruited consecutively from nine movement disorder centers across Germany (Aachen, Bonn, Dresden, Frankfurt/Main, Kassel, Kiel, Marburg, and Tübingen). Inclusion criteria were age between 45 and 80 years and a diagnosis of idiopathic PD based on the UK Parkinson's Disease Society Brain Bank criteria (Hughes et al., 1992). The study included PwPD with cognitive functions within the demographically adjusted norms (PD-NC), with PD-MCI, as well as with PD-D. Cognitive status diagnosis followed diagnostic criteria available at the time of study set-up. Specifically, PD-MCI is defined according to criteria by Petersen (2004), requiring (1) subjective complaint of cognitive decline reported by the patient and preferably supported by a reliable source, (2) minimal impact of the decline on day-to-day functioning and the absence of dementia (both primarily based on clinical interview and history), and (3)

objective evidence of cognitive abnormalities that cannot be simply attributed to age (Balzer-Geldsetzer et al., 2011). PD-D is defined according to criteria by the MDS (Dubois et al., 2007; Emre et al., 2007) and includes cases of probable and possible PD-D. Exclusion criteria included a) a diagnosis of or evidence for atypical Parkinson syndromes (e.g., multiple system atrophy, progressive supranuclear palsy, cortical-basal degeneration), b) other causes of dementia based on clinical grounds (e.g., AD, vascular dementia, frontotemporal dementia, Creutzfeldt-Jakob disease, Huntington's Disease), c) severe cognitive impairment that impedes consent, d) medical and ethical reasons in relation to the morphological and neurobiological examinations, and e) pregnancy.

2.3.2. Assessments

Table 1

Overview of cognitive test scores included in analyses reported in studies II and III.

Theoretically assumed cognitive domain	Test score
<i>Attention</i>	Digit Span forward ^a
	Brief Test of Attention ^b
	Stroop words reading ^c
	Stroop color naming ^c
	Stroop interference ^c
<i>Executive functions</i>	Semantic Word Fluency ^d
	Phonematic Word Fluency ^d
	Trail Making Test B/A ^d
	Digit Span backwards ^d
	Modified Card Sorting Test categories ^e
	Modified Card Sorting Test non-perservative errors ^e
<i>Memory</i>	Modified Card Sorting Test perservative errors ^e
	Figures Recall ^d
	Verbal Learning ^d
<i>Language</i>	Verbal Recall ^d
	Boston Naming Test ^d
<i>Vissual-spatial functions</i>	Figures Copying ^a
	Leistungsprüfsystem 7 ^f
	Leistungsprüfsystem 9 ^f

Note. ^aHärting et al. (2000). ^bSchretlen et al. (1996). ^cBäumler (1985). ^dPart of the extended Consortium to Establish a Registry for Alzheimer's disease neuropsychological test battery (CERAD+; Schmid et al., 2014). ^eNelson (1976). ^fSturm et al. (1993).

Clinical assessment of patients included questionnaires on demographics, medical history, and medications; patient examinations of health status, neurological status, and severity of PD symptoms; blood sampling for serum and plasma, DNA and RNA; structural magnetic resonance imaging of the brain; self-reported measures of depression, apathy, quality of life/health status; and an extensive neuropsychological test battery. For a detailed list of assessments, please refer to Balzer-Geldsetzer et al. (2011).

The present thesis project focuses on the cognitive test score data of the neuropsychological test battery. Table 1 shows an overview of all DEMPARK/LANDSCAPE cognitive assessments that were included in analyses in studies II and III.

2.4. SUMMARY OF STUDY I

Scharfenberg, D., Ophey, A., Lessmann, A., Folkerts, A.-K., Kromke, K., Stahl, J. & Kalbe, E. (2026). Understanding cognitive domains in Parkinson's disease: A scoping review of empirical studies. *Neuropsychology Review*. <https://doi.org/10.1007/s11065-025-09691-5>

2.4.1. General information

The first study, a scoping review on empirical findings regarding cognitive domains in PD, was published in *Neuropsychology Review*. Research questions, search strategy, and a data charting form were preregistered on December 11th 2023 on *PsychArchives* (Scharfenberg, Ophey, et al., 2023). The manuscript was initially submitted on January 31st 2025, revised in July 2025, and accepted for publication on December 10th 2025.

2.4.2. Scientific contributions

The scoping review was conceptualized by **Daniel Scharfenberg**, Anja Ophey, Jutta Stahl, and Elke Kalbe. The systematic literature search was conceptualized by **Daniel Scharfenberg** and Ann-Kristin Folkerts and conducted by Ann-Kristin Folkerts. Each title and abstract was screened by two reviewers, namely **Daniel Scharfenberg** and Konstanze Kromke; conflicts were resolved by third reviewer Elke Kalbe. **Daniel Scharfenberg** conducted the full-text screening and extracted the data. Extracted data was checked for accuracy and expanded by Amelie Lessmann. Visualizations (Figures and Tables) were created by **Daniel Scharfenberg** and Amelie Lessmann. The project was supervised by Elke Kalbe and Anja Ophey. Jutta Stahl gave advice at

different stages of the project. **Daniel Scharfenberg** drafted the first version of the manuscript. All authors subsequently revised the manuscript for intellectual content and approved the final version. **Daniel Scharfenberg** and Elke Kalbe led the submission process and drafted the revision until final publication.

2.4.3. Abstract

Introduction: Cognitive diagnostics in PwPD are typically based on cognitive domains, describing functional divisions of cognitive functioning, such as memory, attention, or executive functions. However, definitions of cognitive domains, specifying abstract cognitive functions or cognitive tests for each domain – such as the diagnostic criteria for neurocognitive disorder in the DSM or for PD-MCI from the MDS – are based on expert consensus rather than empirical evidence. Additionally, such diagnostic criteria lack harmonization of cognitive domains. For example, verbal fluency is classified as a language task in the DSM guidelines but classified as an executive function tasks in the MDS guidelines. Empirical evidence could be derived from applying dimensionality reduction methods, such as factor analyses, to cognitive test data of PwPD, resulting in empirical dimensions or factors of correlating test scores, possibly representing cognitive domains. Despite the high clinical relevance of cognitive domains, there is no systematic collection of such findings to date.

Objective: With the present scoping review, we aimed to provide an overview about empirical findings of dimensionality reduction analyses of cognitive test scores in PwPD. We defined three key exploratory research questions: i) Which methods were used to empirically evaluate cognitive domain differentiations in PD? (ii) Could previously assumed cognitive domains in PD be reproduced by empirical analyses? (iii) Which cognitive domain models (e.g., MDS, DSM) did the studies use as its theoretical framework?

Methods: We preregistered research questions, search strategy, and the data charting form for this scoping review prior to conducting the final search on *PsychArchives* and adhered to the norms and recommendations as described in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Review (PRISMA-ScR) checklist. We conducted a systematic literature search in two data bases containing medical and psychological sources (Ovid MEDLINE, PsycInfo) to reflect the interdisciplinary nature of the research question. The search string included terms from the three key areas for this research

question, that is a) PD, b) cognition and neuropsychological assessment, and c) dimensionality reduction methods. Eligible sources would contain at least one search term from each area. Studies were further eligible for inclusion in the scoping review if they were original research, included relevant ethical approvals, conducted a statistical analysis to extract a dimensionality structure of cognitive functions based on cognitive test data from a sample of PwPD. After removing duplicates, titles and abstracts were screened by two reviewers, with a third reviewer resolving any arising conflicts. Then, one reviewer scanned full texts for final eligibility of inclusion and extracted the data of interest from the full studies; a second reviewer checked these steps for correctness. Expanding our preregistered data charting form, we also included additional information on verbal fluency tasks, as such tasks are especially affected by fuzzy definitions of cognitive domains. Instead of a risk of bias assessment, we performed a critical appraisal of the included sources of evidence, assessing the completeness of information of interest.

Results: Out of 705 studies that were initially screened for potential eligibility for inclusion, we included 22 studies in the scoping review that met the inclusion criteria. Most studies used exploratory dimensionality reduction methods, mainly PCA and EFA, with high heterogeneity regarding the details of methodological specifications, such as use of extraction or rotation methods. Only five studies used confirmatory methods (CFA, specifically). None of the exploratory analyses could reproduce previously assumed assignments of cognitive test scores to cognitive domains. Similarly, verbal fluency tasks were never assigned to the same cognitive domain that was initially proposed for these tasks. Some CFA results indicated at least partial support for the tested cognitive domain model but were not able to consistently confirm any proposed model. Four out of the 22 studies referred to the MDS criteria and assigned cognitive tests to cognitive domains accordingly, whereas no study referred to the DSM criteria. Instead, studies referred to various concepts for assigning cognitive test scores to domains, such as theoretical models of cognition and intelligence (e.g., the *g*-factor of intelligence), neural mechanisms, or previous empirical findings (e.g., published factor structures from neuropsychological test batteries). A critical appraisal of included studies revealed high rates of missing information, with only one study providing all information of interest. Overall, information were missing regarding demographic information, cognitive status, PD clinical

characteristics, and dimensionality reduction methods, with missingness of information showing highest rates for cognitive status and PD clinical characteristics information.

Discussion: Overall, results of the included studies were highly inconsistent. There are various possible explanations for this finding, such as the use of exploratory dimensionality reduction methods that are known to be hardly replicable, the use of heterogenous and inappropriate method specifications (e.g., regarding rotation methods), variations in neuropsychological test batteries used within these studies, and heterogenous samples of PwPD regarding cognitive status and clinical PD characteristics. In sum, the overview of empirical findings provided by the scoping review emphasizes the current gap between assumptions of cognitive domains and empirical evidence.

Conclusion: The inconsistent empirical evidence regarding cognitive domains in PwPD challenges the validity and reliability of cognitive diagnoses in PwPD, highlighting the need for more empirical research on this issue. Going beyond categorical systems of cognitive functioning, network perspectives on cognition might enhance our understanding of the organization of cognitive functions in PwPD.

2.5. SUMMARY OF STUDY II

Scharfenberg, D., Kalbe, E., Balzer-Geldsetzer, M., Berg, D., Hilker-Roggendorf, R., Kassubek, J., Liepelt-Scarfone, I., Mollenhauer, B., Reetz, K., Riedel, O., Roeske, S., Schulz, J.B, Storch, A., Trenkwalder, C., Witt, K., Wittchen, H.-U., Dodel, R. & Ophey, A. (2025). A network perspective on cognition in individuals with Parkinson's disease. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, 17(1), e70091. <https://doi.org/10.1002/dad2.70091>

2.5.1. General information

The second study constitutes an empirical analysis of cross-sectional data to extract a cognitive domain structure based on a psychometric network model of cognitive test scores and was published in *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*. The manuscript was initially submitted on September 30th 2024, revised in December 2024, and accepted for publication on January 20th 2025.

2.5.2. Scientific contributions

The analyses of this dissertation subproject are based on data from the previously described DEMPARK/LANDSCAPE study. Monika Balzer-Geldsetzer, Daniela Berg, Rüdiger Hilker-Roggendorf, Jan Kassubek, Inga Liepelt-Scarfone, Brit Mollenhauer, Kathrin Reetz, Oliver Riedel, Sandra Roeske, Jörg B. Schulz, Alexander Storch, Claudia Trenkwalder, Karsten Witt, Hans-Ulrich Wittchen, Richard Dodel and Elke Kalbe were involved in the conceptualization and data acquisition of the the DEMPARK/LANDSCAPE study. The present subproject was supervised by Anja Ophey and Elke Kalbe. **Daniel Scharfenberg**, Anja Ophey and Elke Kalbe conceptualized the study objectives and analysis plan. **Daniel Scharfenberg** conducted the statistical analysis and visualization of findings. **Daniel Scharfenberg**, Anja Ophey, and Elke Kalbe interpreted the results. **Daniel Scharfenberg** drafted the first version of the manuscript. All authors revised the manuscript for intellectual content and approved the final version of the manuscript. **Daniel Scharfenberg** and Anja Ophey led the submission process and drafted the revisions until final publication.

2.5.3. Abstract

Introduction: Existing literature shows a considerable gap between guidelines for cognitive diagnostics in PwPD and the empirical evidence for cognitive domains, mainly derived from EFA and PCA. Building upon psychometric network analysis, EGA allows to identify a dimensionality structure of cognitive functioning while modelling cognitive functioning as a complex system of associated cognitive test score. To date, there are no studies applying EGA to cognitive test data of PwPD to investigate the structure of cognitive functioning by taking a network perspective on cognition.

Objective: With this empirical study, we aimed to assess the cross-sectional dimensionality structure of cognitive functioning in PwPD in order to enrich the discussion about the definition of cognitive domains in cognitive diagnostics for PwPD. Further, we aimed to compare the dimensionality structure derived from EGA with a theoretically assumed cognitive domain structure that was previously applied to the neuropsychological test battery. We then aimed to conceptually replicate our findings using data from cognitively healthy people without PD.

Methods: For this study, we analyzed baseline data of the DEMPARK/LANDSCAPE study. The final sample size consisted of $N = 698$ PwPD with different cognitive statuses ($n = 282$ people with PD-NC, $n = 314$ PwPD with PD-MCI, $n = 102$ PwPD with PD-D). Using 19 cognitive test scores from theoretically assumed domains attention, executive functions, memory, language, and visuospatial functions, we applied EGA with the Louvain algorithm to a glasso-regularized gaussian graphical model of cognitive test scores to identify the dimensionality structure. We computed network loadings for the EGA dimensionality structure and applied bootstrapping to assess the stability of results. We compared the EGA dimensionality structure and the theoretically assumed cognitive domain structure both qualitatively and quantitatively based on a CFA with using model fit indices TEFI, χ^2 , CFI, and RMSEA. Following the qualitative comparison, we performed UVA to identify and eliminate redundancy between test scores within the test battery based on the weighted topological overlap. After UVA, we reanalysed the reduced data following the same analytic procedures as outlined before. To provide a conceptual replication of our findings, we applied the same analytic procedures to data derived from a large systematic review and meta-analysis containing data from $N = 60,398$ people with healthy cognition without PD across 52 studies.

Results: The EGA identified five dimensions of cognitive test scores within the DEMPARK/LANDSCAPE data. Quantitatively, the EGA dimensionality structure showed consistently better model fit than the structure of theoretically assumed domains. The network model showed strong associations between cognitive test scores from the same test paradigms (e.g., digit span forward and backward; copying figures and recalling figures; subscores of the card sorting test); such test scores were consistently assigned to the same EGA dimensions, even if they were previously assumed to represent different cognitive domains. UVA revealed considerable redundancy between such test scores. After UVA, a reanalysis of the now reduced data yielded a unidimensional structure. The findings were conceptually replicated using data from people with healthy cognition without PD.

Discussion: Strong associations between cognitive test scores from the same test paradigm suggest influence of method variance, that is, variance arising from similar instructions, stimuli, or evaluation procedures. After reducing redundancy between test scores, EGA resulted in a unidimensional network structure, which can be interpreted in light of a network perspective

on cognition rather than a categorical system of latent cognitive domains. The conceptual replication using data from people with healthy cognition without PD suggests that our findings are not specific to PD but might reflect a general issue of cognitive diagnostics.

Conclusion: Findings of the present study suggest that cognitive functioning may be better described as a complex system of interconnected cognitive functions, questioning the concept of categorical cognitive domains. Consequently, the results challenge the validity and reliability of cognitive subtype diagnoses not only in PwPD but in all populations that are assessed based on the idea of cognitive domains.

2.6. SUMMARY OF STUDY III

Scharfenberg, D., Kalbe, E., Ophey, A., Balzer-Geldsetzer, M., Berg, D., Hilker-Roggendorf, R., Kassubek, J., Liepelt-Scarfone, I., Mollenhauer, B., Reetz, K., Riedel, O., Roeske, S., Schulz, J.B, Storch, A., Trenkwalder, C., Witt, K., Dodel, R. & Deserno, M. (2026). Temporal dynamics of cognitive functioning in people with Parkinson’s disease. *npj Parkinson’s disease*, 12, 86. <https://doi.org/10.1038/s41531-026-01338-3>

2.6.1. General information

The third study, investigating the temporal dynamics of cognitive functioning in PwPD, was submitted to *npj Parkinson’s disease* on December 5th 2025, revised in February and March 2026 and accepted on March 23th 2026.

2.6.2. Scientific contributions

The analyses of this dissertation subproject are based on data from the previously described DEMPARK/LANDSCAPE study. Monika Balzer-Geldsetzer, Daniela Berg, Rüdiger Hilker-Roggendorf, Jan Kassubek, Inga Liepelt-Scarfone, Brit Mollenhauer, Kathrin Reetz, Oliver Riedel, Sandra Roeske, Jörg B. Schulz, Alexander Storch, Claudia Trenkwalder, Karsten Witt, und Richard Dodel were involved in the conceptualization and data acquisition of the the DEMPARK/LANDSCAPE study. The present subproject was supervised by Marie Deserno, Elke Kalbe, and Anja Ophey. **Daniel Scharfenberg**, Marie Deserno, Elke Kalbe, and Anja Ophey conceptualized the study objectives and analysis plan. **Daniel Scharfenberg** conducted the

statistical analysis and visualization of findings. **Daniel Scharfenberg**, Marie Deserno, Elke Kalbe, and Anja Ophey interpreted the results. **Daniel Scharfenberg** drafted the first version of the manuscript. All authors revised the manuscript for intellectual content and approved the final version of the manuscript. **Daniel Scharfenberg** and Marie Deserno led the submission process. **Daniel Scharfenberg**, Marie Deserno, Elke Kalbe, and Anja Ophey drafted the revisions until final publication.

2.6.3. Abstract

Introduction: Guidelines for cognitive diagnostics such as the DSM diagnostic criteria for NCD or the MDS diagnostic criteria for PD-MCI define cognitive domains but do not include information about how cognitive functions and domains evolve over time, implicitly assuming temporally stable cognitive domains. Information about trajectory of cognitive domains are scarce, as existing literature mainly focuses on conversion between cognitive statuses, neglecting domain-specific cognitive decline and the coupling of different cognitive domains. Similarly, empirical evidence regarding cognitive domains in PwPD is based on cross-sectional data and methods, such as factor analyses. Network approaches could be a promising method to identify temporal (re)organization of cognitive functioning and dependencies between cognitive domains in cognitive decline.

Objective: With this study, we aimed to identify the temporal dimensionality structure of cognitive functioning in PwPD, that is, identify clusters of cognitive test scores that show similar cognitive change over time. We then aimed to compare the temporal dimensionality structure with a dimensionality structure from cross-sectional data and a theoretically assumed cognitive domain structure. Further, we aimed to explore dynamic coupling between the identified temporal dimensions, that is, which dimensions predict other dimensions (or themselves) at the next time point of assessment.

Methods: We analyzed longitudinal cognitive test data from the DEMPARK/LANDSCAPE study, spanning four time points of yearly assessments. The final sample included $N = 355$ PwPD with different cognitive statuses ($n = 185$ PwPD with PD-NC, $n = 145$ PwPD with PD-MCI, and $n = 25$ PwPD with PD-D at baseline). First, we applied dynEGA with the Louvain algorithm to the 19 cognitive test scores included in the neuropsychological test battery to identify the dimensionality structure based on a GGM of first-order derivatives of the cognitive test scores,

indicating rate of change over time. We compared the resulting dynEGA dimensionality structure with the cross-sectional dimensionality structure identified in study II and the theoretically assumed cognitive domain structure that was applied previously to the cognitive test battery. We also performed linear mixed-effects model with time and either the dynEGA dimensions or the theoretically assumed cognitive domains as fixed effects and a random intercept predicting the MMSE total score in order to evaluate and compare model fit of both structures. Then, we estimated panel GVAR models on dynEGA dimension mean scores in order to explore dynamic couplings between identified dimensions.

Results: The dynEGA identified five dimensions: *visuoconstruction*, *executive/visual-spatial functions*, *card sorting/cognitive flexibility*, *attention/processing speed*, and *verbal functions*. The dynEGA dimensions' composition differed from both, the cross-sectional EGA dimensions identified in study II and the theoretically assumed cognitive domain structure. The linear mixed-effect model revealed better model fit in predicting the MMSE score for the dynEGA dimensions compared with the theoretically assumed domains. The temporal GVAR model showed two clusters of dimensions: one cluster of *executive/visual-spatial functions*, *attention/processing speed*, and *verbal functions* showing that *executive/visual-spatial functions* and *attention/processing speed* mutually predict each other and themselves positively, whereas *verbal functions* positively predicts themselves and *executive/visual-spatial functions*; another cluster showed a negative directed association from *card-sorting/cognitive flexibility* toward itself and *visuoconstruction*.

Discussion: The findings suggest that cognitive organization may change dynamically over time, although not reflected in current diagnostic guidelines, possibly reflecting a differential, staged trajectory of cognitive decline in PwPD. The dynEGA dimensions showing better model fit compared to the theoretically assumed cognitive domains for predicting MMSE score highlights the potential of including temporal information for improving diagnostic accuracy. Results from the GVAR can be related to the DSH, confirming a separation between early executive dysfunctions of the fronto-striatal path and later decline of visual-spatial abilities of the posterior-cortical path.

Conclusion: The results challenge the assumption of temporally stable cognitive domains, potentially limiting the validity and reliability of cognitive diagnostics in PwPD. Further research

is needed to confirm the predictive utility of cognitive guidelines including temporal information for diagnostics and accuracy of cognitive and other clinical outcomes. Longitudinal network methods are promising tools for analysing complex temporal relationships of cognitive functioning in PwPD, possibly reflecting disease-specific mechanisms.

CHAPTER 3 - GENERAL DISCUSSION

The aim of the present thesis project was to empirically evaluate the concept of cognitive domains through the lens of a network perspective. Further, the thesis aims to contribute to forming an empirically-based judgement about the validity and reliability of cognitive diagnoses based on cognitive domains. For that, we provided an overview of existing empirical findings on cognitive domain structures PwPD by performing a scoping review (study I), identified the cross-sectional empirical dimensionality structure of cognitive test scores in a large sample of PwPD (study II), and identified the longitudinal empirical dimensionality structure of cognitive test scores PwPD to test the assumption of temporally stable cognitive domains (study III).

In this general discussion, I will summarize the main findings of the thesis project in light of the defined specific research questions (see chapter 2.1.) as well as their implications for the general aim of this project. Specific discussion points regarding methodological aspects are discussed in the original publications. Nonetheless, this discussion also includes a chapter on general strengths and limitations of the present thesis project. Finally, I will discuss implications of the findings for future research and possible clinical applications.

3.1. STUDY I – SCOPING REVIEW OF EMPIRICAL STUDIES

- a) What empirical evaluations of cognitive domain structures exist so far and how consistent are they with theoretically and experts' consensus based diagnostic guidelines?*
- b) If studies categorized cognitive tests into cognitive domains on a theoretical basis, were they able to reproduce this categorization in their analyses?*
- c) Did studies refer to the DSM definition of cognitive domains or the MDS criteria on diagnosing PD-MCI?*

We aimed to provide an overview of empirical studies that have applied dimensionality reduction methods to cognitive test data from PwPD and compare their results with the theoretically assumed cognitive domain structures outlined in the guidelines of the MDS PD-MCI guidelines or the DSM criteria for NCD. Specifically, we examined which methods have been employed in such empirical studies, whether the studies successfully reproduced hypothesized cognitive domain structures, and whether they referenced the MDS or DSM

guidelines. Below, I discuss how the empirical database identified in our scoping review contributes to evidence for cognitive domain structures.

3.1.1. Statistical methods of existing empirical sources

The scoping review on empirical studies on cognitive domain structures in PwPD included 22 sources of evidence that met the preregistered inclusion and exclusion criteria. Most studies employed exploratory dimensionality reduction methods, primarily PCA or EFA, whereas only five studies employed confirmatory dimensionality reduction methods, specifically CFA.

The findings indicate that the use of methods in the included studies often contradict recommendations for dimensionality reduction methods. For example, most exploratory studies using PCA or EFA applied orthogonal rotation methods, assuming independence between the resulting factors or components (Costello & Osborne, 2005). However, this assumption is unreasonable from both theoretical and empirical perspectives, as cognitive domains or clusters of cognitive test scores are typically correlated (van der Maas et al., 2006). Oblique rotation is recommended instead, as it yields more accurate and reproducible results for correlated factors/components, and produces similar outcomes to orthogonal rotation when factors/components are uncorrelated (Costello & Osborne, 2005).

In addition, using exploratory dimensionality reduction methods such as PCA or EFA might be problematic. While these methods are widely used, they have been shown to be heavily influenced by sample-specific variance, resulting in non-replicable factor/component models (Floyd & Widaman, 1995). A simulation study has also shown that CFA is more accurate in identifying the true number of factors in intelligence-like data by assessing model fit across different factor models (Keith et al., 2016). Accordingly, guidelines advise against using EFA or PCA if it is possible to theoretically or empirically derive and test factor structures using CFA (Costello & Osborne, 2005; Henson & Roberts, 2006). Regarding cognitive domain structures, this approach would have been the most appropriate. For example, Agelink van Rentergem et al. (2020) used CFA to compare different models of cognitive organization, such as the Cattell-Horn-Carroll model (Schneider & McGrew, 2018), in a combined sample of over 60,000 individuals with healthy cognition.

Importantly, CFA is the most appropriate dimensionality reduction method only if we assume cognitive organization is best represented by latent factors. Other concepts that reject the idea of latent cognitive factors require different statistical methods to align with theoretical assumptions, such as psychometric network analysis in combination with network perspectives on cognition (e.g., the mutualism hypothesis of cognition van der Maas et al., 2006).

3.1.2. Inconsistent findings of cognitive domain structures

The scoping review revealed that no exploratory analyses could reproduce a formerly assumed cognitive domain structure. Confirmatory analyses only showed partial support for good model fit across different model fit indices. Overall, findings on cognitive domain structures in the summarized empirical studies were highly inconsistent.

As discussed, this inconsistency can be attributed to the inappropriate use of exploratory dimensionality reduction methods, specifically EFA and PCA, which lead to non-replicable results. Additionally, the included empirical studies showed high heterogeneity in other methodological domains beyond the choice of dimensionality reduction methods. Examples of this heterogeneity include the composition and comprehensiveness of the cognitive test batteries, the sample size (ranging from 21 – 1738), the cognitive status of included PwPD (which often did not differentiate between PD-NC, PD-MCI, and PD-D), and other PD-specific clinical characteristics of the sample such as Hoehn & Yahr stages (Hoehn & Yahr, 1967) and Unified Parkinson's Disease Rating Scale part III scores (Fahn, 1987) as indicators for PD-specific motor impairment. Furthermore, such information, especially regarding clinical characteristics, was often not reported at all. Consequently, findings are not only inconsistent but also difficult to summarize and group according to these variables. This obstacle hinders the detection of meaningful patterns in the results, which may be masked by heterogeneous methods.

3.1.3. Value of diagnostic guidelines for cognitive domain definitions

From the 22 studies included in the scoping review, only four referred to the MDS diagnostic criteria for PD-MCI and none explicitly referred to the DSM cognitive guidelines for NCD. Instead, we observed a great variety of concepts that had been used to categorize cognitive test scores, for example, the *g*-factor of intelligence, neural correlates, or empirical

findings from previous studies or preceding exploratory analyses. These findings reflect that most studies were not explicitly interested in identifying cognitive domains, but stated other aims for their analyses. Even if taking into account that several studies included in the scoping review have been published after publication of the MDS and DSM guidelines, ten studies did not refer to MDS or DSM guidelines compared to four which did. Thus, it is striking that most neuropsychological test batteries appear not to be composed according to existing diagnostic guidelines such as MDS PD-MCI criteria, using either different theoretical concepts or no explicit foundation for their decisions at all. As discussed in chapter 1.3.1., expert opinions on cognitive domains can add to the inconsistency of cognitive subtyping diagnoses due to inconsistent cognitive domain definitions. In chapter 3.5.2., we further discuss the extent of such cognitive subtype differences due to different cognitive domain definitions.

3.2. STUDY II – CROSS-SECTIONAL STRUCTURE OF COGNITIVE DOMAINS

What is the empirical dimensionality structure of cross-sectional cognitive test scores in a sample of PwPD and how does it differ from a theoretically assumed cognitive domain structure?

In an empirical analysis, we aimed to identify the dimensionality structure of cognitive test scores in a sample of PwPD with mixed cognitive statuses. The study adopts a network perspective by employing psychometric network analysis. We compared the resulting structure to a theoretically assumed cognitive domain structure that was used to categorize the cognitive test scores in the DEMPARK/LANDSCAPE study. In the following, I will discuss the findings in light of their significance for evaluating the concept of cognitive domains in PwPD.

3.2.1. Method variance in cognitive test scores

The initial empirical dimensionality analysis of cognitive test scores from PwPD in the DEMPARK/LANDSCAPE study, conducted using EGA, could not reproduce the theoretically assumed cognitive domain structure previously applied to the cognitive test battery. Upon comparing both models, it is evident that cognitive test scores with similar instructions or dependent stimuli (e.g., digit span tasks forward and backward; copying and recalling figures) are often grouped together in the EGA solution, even if they were assumed to measure different cognitive domains. This finding suggests a strong bias from method variance, which

describes the tendency for variables from the same test to correlate because their responses are elicited by the same stimuli or methodology (Larrabee, 2003). Importantly, the effect of method variance might have significant clinical relevance for cognitive subtyping in cognitive diagnostics. Specifically, method variance can mask the variance of interest, which stems from measuring different cognitive functions, potentially leading to invalid measurement. Consequently, cognitive test scores depending on the same stimuli or methodology are highly correlated while still being interpreted as measuring distinct underlying cognitive functions. By overlooking the empirical association between test scores due to method variance, cognitive diagnostics risk misinterpreting low performance in cognitive test scores as impairments of distinct cognitive functions. This is because there is a high likelihood that both test scores will show very similar results. Thus, high correlations between test scores can be seen as redundancy, as including a second test score that is likely to be similar to the first one would not provide a substantial gain of information.

The issue of possibly redundant test scores is already acknowledged in the MDS diagnostic guidelines for PD-MCI, stating that “two highly similar tests (e.g., two list learning tests or two story recall tests) should not be used to meet the MCI criterion of two test-score abnormalities. Similarly, highly correlated scores from the same test (e.g., immediate and delayed recall of a word list) should not be used to meet the criterion of two test abnormalities” (Litvan et al., 2012). Interestingly, both examples refer to pairs of cognitive test scores typically assumed to belong to the same cognitive domain. However, our findings suggest that this warning should be extended by explicitly stating that high correlations between cognitive test score may be attributed to method variance and may problematically affect pairs of test scores assumed to measure cognitive functions from different cognitive domains, such as visuo-construction of figures (visual-spatial functions) and delayed recall of these figures (memory). As many studies do not refer to the MDS diagnostic guidelines (see chapter 1.2.1.), it is unclear how often this important warning is considered by clinicians and researchers. While some studies follow the suggestion (e.g., Lawrence et al., 2016) and even explicitly consider the warning (e.g., Seubert-Ravelo et al., 2016), others do not.

3.2.2. Unidimensional structure of cognitive test scores

Beyond the clinical relevance discussed, the redundancy between cognitive test scores posed another problem for addressing the research question on the structure of cognitive domains in the present dissertation project: High-correlations between cognitive test scores potentially biased results of the EGA, creating misleading minor dimensions based on redundant scores (Christensen et al., 2023). To address this, we systematically identified and eliminated redundant test scores using UVA (Christensen et al., 2023). After applying UVA, we performed EGA again with reduced data, resulting in a unidimensional network structure.

In the scoping review (Scharfenberg, Ophey, et al., 2026), we found only one study that derived a one-factor model from EFA (Shirzadi et al., 2018). However, this study included the fewest cognitive test scores in its EFA compared to the other studies included in the scoping review and did not appear to include redundant test scores. Our findings suggest that by inflating our test batteries with redundant test scores – based on the assumption that we will find distinct cognitive domains – we potentially bias our dimensionality reduction analyses.

The unidimensional network structure can be interpreted in the context of two theoretical models explaining cognition and intelligence: the *g*-factor of intelligence (Spearman, 1927) and the mutualism hypothesis of intelligence (van der Maas et al., 2006). Both theories can explain both the positive manifold and a unidimensional structure of cognitive test scores but make different assumptions: The *g*-factor of intelligence assumes a latent factor of intelligence that underlies all cognitive functions and abilities. This explains the typical empirical finding of correlated cognitive functions, that is, the positive manifold. The mutualism hypothesis of intelligence explains the positive manifold by assuming positive reciprocal associations between cognitive process. It can be interpreted as a network theory of intelligence. The mutualism hypothesis is a developmental theory, positing that the positive manifold emerges thorough reciprocal causation between different cognitive functions during development (van der Maas et al., 2006).

There are several arguments that favor interpreting the results in light of the mutualism hypothesis. First, the results of the loadings comparison test (Christensen & Golino, 2021a), an algorithm based on neural networks that was trained to predict whether data were generated from a latent factor model or a network model, suggested that the data are more likely to have

been generated from a network model rather a latent factor model. Thus, the results support the application of psychometric network analysis and EGA and favor interpreting the results in the light of network models of cognitive functioning, such as the mutualism hypothesis. Second, another study compared psychometric network models of cognitive test scores with traditional factor analyses in samples of cognitively healthy adults and children. The study found that psychometric network models showed a better model fit than latent factor models of *g* (Kan et al., 2019). The authors of this study thus conclude that empirical evidence argues against the theory of a *g*-factor of intelligence, favoring the mutualism theory of intelligence. In sum, we too interpret our findings in the light of network models of cognition rather than a latent factor model of cognitive domains or an underlying *g*-factor. The conceptual replication performed with data of cognitively healthy people strengthens our results and interpretation, suggesting that our findings do not reflect PD-specific cognitive structures but are potentially relevant to all cognitive diagnostics irrespective of the (clinical) population at interest.

3.2.3. Implications of a network perspective on cognition

Assuming cognitive functioning as a complex system or network model has relevant implications compared to the use of latent factor models. Network models allow the visualization of multivariate associations between cognitive test scores simultaneously. This enables us to capture important characteristics and regularities within the cognitive functioning network at a glance, such as stronger correlations due to method variance between test scores using the same stimuli or instructions, as discussed above. By acknowledging the dependencies between cognitive test scores, network perspectives highlight a critical limitation of cognitive assessment: We are typically unable to capture isolated cognitive functions. Consequently, it seems logical to acknowledge that categorical concepts, such as cognitive domains, may not be the best models for representing a complex system like cognition. However, current guidelines and criteria for cognitive diagnostics in PwPD and in general are geared towards the concept of cognitive domains. There are currently no appropriate metrics for characterizing and quantifying cognitive performance based on psychometric network analyses. Possible future directions on this issue and clinical implications are discussed in chapter 3.5.

3.3. STUDY III – TEMPORAL DYNAMICS OF COGNITIVE FUNCTIONING

Are cognitive domain structures temporally stable in PwPD?

- a) What is the empirical dimensionality structure of longitudinal cognitive test scores in a sample of PwPD and how does it differ from a theoretically assumed cognitive domain structure and the empirical dimensionality structure of study II?*
- b) How are longitudinal cognitive dimensions coupled, that is, which dimensions predict each other longitudinally?*

In further empirical analyses, we aimed to investigate the temporal dynamics of cognitive functioning in PwPD. In this study, we applied psychometric network analysis to longitudinal cognitive test data and identified dimensionality within the network model using dynEGA. In addition, we used GVAR analyses to identify dynamic coupling between the previously identified cognitive dimensions. In the following chapter, I will discuss the findings of this study and their implications for the use of cognitive domains in neuropsychological clinical practice and research.

3.3.1. Dynamic organization of cognitive functioning

The clusters identified by dynEGA in this study differed from the crossEGA structure identified in study II (Scharfenberg et al., 2025) and the theoretically assumed cognitive domain structure used in the DEMPARK/LANDSCAPE study (Kalbe et al., 2016). Differences between cross-sectional and longitudinal dimensionality structures might be explained by Simpson's paradox: correlations observed in one level of analysis can be reversed when additional explanatory variables are included (Kievit et al., 2013). In this case, correlations observed in cross-sectional data can potentially reverse or weaken when additional time points of assessment are considered, focusing on within-subject effects rather than between-subject effects. Following a qualitative comparison of dynEGA and crossEGA dimensionality structures, findings indicated reduced bias from method variance in the dynEGA structure compared to the crossEGA structure. With dynEGA dimensions reflecting clusters of cognitive test scores showing similar rates of change over time, longitudinal dynEGA dimensions demonstrate the sequential, staged proregression of cognitive decline in different cognitive functions in PwPD.

The longitudinal dimensions thus can be interpreted as reflecting a deeper, more complex system than cross-sectional task similarity as observed in the crossEGA results of study II.

To identify such patterns, it is necessary to gain a deeper understanding of what cognitive test scores actually reflect. By mapping involvement of cognitive processes in cognitive tasks in detail, we are able to back up empirical findings of dimensionality reduction methods by theoretical concepts or mutual task features. In turn, a deeper understanding of cognitive clustering may inform us about mutual cognitive processes involved in cognitive tasks that seemed unrelated previous to empirical results showing their statistical association. This includes the interpretation of network and dimensionality indices, such as network loadings. As network loadings reflect each node's contribution to the identified dimensions, cross-loadings – that is, high network loadings for more than one dimension – may provide insights into differential cognitive involvement during a single task.

Similar to the interpretation of the previous crossEGA findings, we do not claim to have identified the “true” cognitive domain structure with the dynEGA structure. The dynEGA structure depends on several data characteristics (e.g., composition of the cognitive test battery, sample population and size) and decisions made during the analysis process. Therefore, specific results of similar studies will presumably differ from the dynEGA structure in this study. Nevertheless, our results serve as another example of the divergence between empirical results and theoretical assumptions regarding the structure of cognitive domains in PwPD. This has important implications for neuropsychological diagnostics and research.

By identifying the temporal reorganization of cognitive functioning, our findings challenge the assumption of temporally stable cognitive domains, which is implicitly made by diagnostic guidelines such as the DSM (American Psychiatric Association, 2013) or the MDS PD-MCI (Litvan et al., 2012) criteria. Ignoring the dynamic cognitive organization may jeopardize the validity and reliability of cognitive diagnostics, such as cognitive subtyping, in PwPD. Moreover, the value of cognitive subtypes extends beyond cognitive diagnostics in clinical neuropsychology to neuropsychological research. For instance, subtype diagnoses are seen as prognostic for clinical disease progression (Wood et al., 2016) and are often linked to potentially relevant diagnostic and prognostic biomarkers. These include neuroimaging measures (Devignes et al., 2022), genetic factors (Fagan & Pihlstrøm, 2017), or digital

biomarkers such as actigraphy data (Donahue et al., 2022). These biomarkers may help identify mechanisms and risk factors of cognitive decline in PwPD. By acknowledging the limitations of diagnostic guidelines based on the assumption of temporally stable cognitive domains, we may improve the quality of cognitive (subtype) diagnoses. Additionally, this approach enhances the quality and validity of findings that link cognitive phenotyping to other data modalities, which is crucial for uncovering PD-specific mechanisms of cognitive decline. As a first step, our results demonstrate that longitudinal dynEGA dimensions show better predictive utility for modelling the total score of brief cognitive screening test MMSE (Folstein et al., 1975) compared to the theoretically assumed domains. This suggests that incorporating longitudinal information can indeed increase diagnostic and prognostic accuracy in neuropsychological research and clinical practice. Future studies should confirm these findings for other cognitive outcomes and investigate whether this also applies to other disease biomarkers, such as motor symptoms of PD, neuroimaging data, genetic factors, or digital biomarkers (e.g., actigraphy data).

Other clinical implications arise for planning of appropriate and effective cognitive training interventions for PwPD. With the call for personalized cognitive training interventions for PwPD (Kalbe et al., 2018), cognitive subtypes come into focus for applying deficit-specific cognitive training interventions (Bruno et al., 2024). Again, improving the validity of cognitive subtypes by considering the temporal cognitive organization might in turn also increase the effectiveness of personalized cognitive interventions in PwPD.

3.3.2. Dynamic couplings of cognitive dimensions

Based on the longitudinal dimensions identified by dynEGA, we analysed dynamic couplings of these dimensions using panel GVAR analysis. This analysis determined whether one dimension predicts another (or itself) in the next measurement. The results revealed a directed negative association from dimension *card-sorting/cognitive flexibility* towards the *visuoconstruction* dimension. Notably, this finding aligns with assumptions of the DSH of cognitive impairment in PD (see chapter 1.1.3.). The negative temporal association between the cognitive dimensions could reflect the postulated separation of early executive deficits of the fronto-striatal path (reflected by the *card-sorting/cognitive flexibility* dimension) from later visual-spatial deficits of the posterior-cortical path. Importantly, the findings suggest that the *visuoconstruction* dimension reflects the proposed posterior-cortical impairments better than

the *executive/visual-spatial functions* dimension, which includes tasks requiring visual-spatial processes of the posterior-cortical path but also require executive functions of the fronto-striatal path. This ambiguity of visual-spatial tasks is also reflected in the network loadings of the dynEGA, showing cross-loading of the Leistungsprüfsystem subtest 9 score with the *attention/processing speed* dimension. This finding adds to existing literature suggesting a) the shared demands of both executive functions of the fronto-striatal path and visual functions of the posterior-cortical path, for visual-spatial tasks (Kehagia et al., 2010, 2013), and b) that visuoconstructive tasks such as Figures Copying and Figures Recall of the CERAD+ (Morris et al., 1989) reflect visual functions of the posterior-cortical path more purely than the ambiguous visual-spatial tasks (Liebermann-Jordanidis et al., 2022).

Importantly, interpretation of the temporal model has to take into account the temporal distance between measurement occasions. In the DEMPARK/LANDSCAPE study, cognitive assessment was performed in yearly intervals. Thus, the temporal model may not capture changes that happen fast than observed by the yearly interval. Instead, the contemporaneous model (see chapter 1.4.1.) can capture such changes, identifying bidirectional predictions between variables within the same measurement occasion after accounting for temporal information (Epskamp, Waldorp, et al., 2018). The contemporaneous model from study III showed similar patterns as the temporal model but features an additional positive edge between *verbal functions* and *card-sorting/cognitive flexibility* and misses the negative edge between *card sorting/cognitive flexibility* and *visuoconstruction*. The similarity between the temporal and contemporaneous effects models indicates that a yearly interval might be an appropriate temporal distance for identifying temporal dynamics of cognitive functioning in PwPD. However, acceleration of cognitive change may differ depending on cognitive status, PD progression, or other clinical characteristics. Therefore, future research should investigate the potential of more frequent measurement in order to capture short-term cognitive dynamics that might occur in PwPD.

In sum, our findings, which match predictions of the DSH, suggest that dynamic couplings may reveal disease-specific mechanisms of cognitive decline. Consequently, the methodological approach demonstrated in this study might also enrich the investigation of disease-specific mechanisms in other clinical samples, such as people with AD. However, due

to the lack of an age-matched control sample, we cannot rule out the possibility that the temporal dynamics reported in this study may instead reflect non-specific aging-related processes.

3.4. GENERAL STRENGTHS AND LIMITATIONS

The main strength of this thesis project is the triad of a scoping review, a cross-sectional, and a longitudinal empirical analysis, taking diverse perspectives on the research question regarding the definition and organization of cognitive domains in PD. The scoping review (study I) provided an overview of existing empirical studies on cognitive domain evaluations in PD. Studies II and III added empirical analyses on the topic, using data from a large cognitive dataset of PwPD and employed both cross-sectional and longitudinal approaches. Together, the studies' perspectives complement each other to draw an elaborate picture on the concept of cognitive domains in PwPD.

Another strength is the use of psychometric network analysis of cognitive test scores to evaluate the empirical basis for cognitive domains in neuropsychological diagnostics in PwPD. Applying psychometric network analysis allows to adequately model cognitive functioning as a complex system of interconnected cognitive functions. This approach advances our understanding of cognitive functioning from categorical systems towards a network perspective. While several studies already exist within the network neuropsychology framework (Ferguson, 2022), the innovation of the present project lies in its clearly defined research question regarding the organization of cognitive domains. Although some studies have applied psychometric network analysis or even EGA (or similar clustering methods) based on psychometric network analysis to cognitive test data from people with cognitive impairment (e.g., Longo et al., 2024 in PD; Grunden & Phillips, 2024b; Tosi et al., 2024 in AD), they fell short of drawing conclusions regarding the concept of cognitive domains or clinical implications.

For study II and study III, we analysed data from the DEMPARK/LANDSCAPE study (Balzer-Geldsetzer et al., 2011), a large, completed, observational, prospective multi-center cohort study. The study initially aimed to characterize the natural course of cognitive decline in PwPD. Initially including over 700 PwPD at baseline and providing up to seven yearly time points of assessments, the data allowed for employing EGA methods with appropriate statistical

power, evidenced by stable results of sensitivity analyses and the conceptual replication of study II's findings. In addition, the data allowed for analysis of both cross-sectional and longitudinal data. By this, it was possible to compare cross-sectional and longitudinal results derived from the same underlying statistical models applied to the same data structure, clinical sample and neuropsychological test battery composition. As the scoping review (study I) showed, results from empirical dimensionality reduction analyses are typically difficult to compare and synthesize across different studies due to high heterogeneity in statistical approaches, clinical characteristics, and neuropsychological test batteries. Furthermore, the longitudinal data of the DEMPARK/LANDSCAPE study allowed for analyzing the temporal dynamics of cognitive functioning, which is typically neglected by cross-sectional data and statistical methods.

However, the sample size of the DEMPARK/LANDSCAPE study did not allow for separate analysis of cognitive status groups (PD-NC, PD-MCI, PD-D). Separate analysis of these groups would have allowed for a more refined understanding of cognitive organization shifts along disease progression. One study that applied psychometric network analysis to cognitive test data from PwPD revealed differences between the cognitive network models of the PD-MCI group and the group of PwPD without cognitive impairment, with the PD-MCI network appearing less sparse and showing weakened relationships between nodes (Longo et al., 2024). Importantly, this study did not employ EGA or any other clustering method to make inferences about cognitive domain organization. Some other studies applied EGA to separate cognitive status groups across the AD risk states and found inconsistent results for the cognitive status groups (Grunden & Phillips, 2024b; Tosi et al., 2024). However, these studies applied EGA below the simulation-based sample size recommendations (Golino et al., 2020), likely yielding unstable results with very limited interpretability. Thus, future studies will need adequate sample sizes to apply EGA to cognitive status subgroups separately.

For the scoping review reported in study I, we preregistered the research questions, search strategy, and data extraction sheet (Scharfenberg, Ophey, et al., 2023), following recommendations of the PRISMA-ScR checklist (Tricco et al., 2018). However, we did not preregister analytic choices for study II and III. The lack of preregistrations can be seen as a main limitation of the empirical studies, as psychometric network analysis requires a multitude

of analytic decisions that could potentially bias the conclusions drawn from the results. Although preregistrations are often common practice today in psychological research, preregistrations of psychometric network analysis studies remain rare. A recent preprint found that only 3.7% of psychological studies employing network analysis from 2023 to 2025 included a detailed analysis plan (Hoekstra et al., 2025), compared to about 40% observed in 2024 in the general field (Pfadt et al., 2025). Recently, during the progress of this dissertation project, the field has started to shift more towards confirmatory approaches with network analysis frameworks (Du et al., 2025). Additionally, other initiatives aim to reduce bias from undefined analytic choices, such as introducing preregistration templates for both, cross-sectional (Burger et al., 2024) and longitudinal (Freichel et al., 2024) network analysis, or analysis blinding (Hoekstra et al., 2025).

Hence, study II and III followed an exploratory approach. In the context of factor analyses, common guidelines recommend to employ confirmatory analyses, such as CFA, whenever it is possible to derive a hypothesis about the structure in question from theory or previous findings (Costello & Osborne, 2005; Henson & Roberts, 2006). This is because EFA and PCA are known to often yield unstable results due to not separating model-variance from residual variance, biasing results by sample specific variance (Floyd & Widaman, 1995). Although the specific statistical issue of EFA and PCA does not apply to EGA, employing exploratory methods still risk yielding false-positive results that are in turn interpreted as “true” structures of cognitive functioning. Importantly, we do not claim to have found such “true” structures but rather highlight the dissociation between theoretical assumptions of cognitive domains and empirical findings. The use of EGA as an exploratory method in study II and III can still be justified for various reasons. First, we explicitly aimed to apply a network perspective on cognitive functioning as an alternative to factor models that assume latent cognitive domain factors. Choosing psychometric network analysis as the appropriate statistical method, confirmatory methods regarding clustering in psychometric network models were rare and unvalidated at the time of planning the thesis project. Not until recently has a confirmatory approach that evaluates fit indices of structural equation modeling has been published (Du et al., 2025). Second, dynEGA allowed us to investigate temporal dynamics of cognitive functioning. Third, with EGA methods allowing the use of the same statistical method to both

cross-sectional (Golino & Epskamp, 2017) and longitudinal data (Golino et al., 2022), its use increased consistency of the approaches within the present thesis.

Another limitation is the uncertainty regarding whether the presented findings on the structure of cognitive domains are specific to PD or reflect aging-related processes rather than disease-specific mechanisms. However, our findings suggest both explanations for different aspects of the findings. On the one hand, the conceptual replication of study II in people with healthy cognition indicates that the issue of fuzzy definitions for cognitive domains and the possibility of modelling cognition as a network model of interconnected cognitive functions are relevant not only in PD but also in cognitively healthy populations and presumably in other clinical populations. On the other hand, the GVAR findings, which match predictions from the DSH, suggest that temporal dynamics (i.e., both cognitive reorganization of cognitive clustering and temporal couplings of cognitive clusters) may reflect disease-specific mechanisms. However, more research in various populations is needed to answer this question.

In addition, it is not possible with our analyses to differentiate between effects of method variance and conceptual variance, that is, variance reflecting shared cognitive processes. In study II, we employed UVA to identify and eliminate redundancy of cognitive test scores after noticing the effects of method variance. However, UVA does not differentiate between method variance and conceptual variance. Differentiating between the method variance and conceptual variance might increase the validity of dimensionality reduction methods to reflect shared cognitive processes. Importantly, this limitation is not specific to EGA but also applies to other dimensionality reduction methods, such as factor analyses.

3.5. IMPLICATIONS AND FUTURE DIRECTIONS

The findings of the present dissertation project have important implications for both scientific research and clinical practice. Some of these implications have been briefly mentioned before but will be discussed in more detail in the following chapter.

3.5.1. Implications for future research

Findings from all three studies in this dissertation project highlight the considerable gap between expert consensus on cognitive domain definitions – reflected, for example, in guidelines for cognitive diagnostics – and the lack of empirical evidence for these assumptions

about cognitive domain structures. The scoping review (study I) revealed that existing studies a) rarely explicitly addressed the issue of heterogeneous cognitive domain definitions, b) primarily used exploratory methods with heterogeneous specifications (e.g., regarding extraction or rotation method), and c) consequently yielded heterogeneous results that did not support any specific cognitive domain structure as a promising solution. Future research on cognitive domains should thus shift its focus toward confirmatory approaches to bridge the gap between theoretical assumptions and empirical evidence. Specifically, different cognitive domain structures should be directly compared within the same sample of PwPD. This comparison should include structures derived from diagnostic guidelines, assumptions derived from theoretical frameworks such as Cattell-Horn-Carroll models (Schneider & McGrew, 2018) or the *g*-factor of intelligence (Spearman, 1927), and findings from previous exploratory analyses of both EFA and EGA. Similar work has already been conducted for people with healthy cognition (Agelink van Rentergem et al., 2020), serving as an exemplary work to adapt for the PD population in the future.

Beyond evaluating of how well cognitive domain models fit empirical data on cognition, future studies should also validate the utility of well-fitting models for diagnostic and prognostic accuracy. That is, they should confirm that cognitive domain structures can serve as a reliable foundation for diagnostic criteria that can validly and reliably detect cognitive impairment in PwPD. Furthermore, research should show whether these structures are useful in predicting cognitive decline and other clinically relevant outcomes, such as motor symptoms or digital biomarkers.

Findings from study III demonstrated that the organization of cognitive functioning may change dynamically over time, contradicting the implicit assumption of temporally stable cognitive domain definitions from diagnostic guidelines. Future studies should further investigate the coupled changes of cognitive functions, moving beyond categorical approaches that aim to map conversion between cognitive statuses. A better understanding of the sequential decline of cognitive functions in PwPD could ultimately enhance the prognostic accuracy of cognitive decline. This knowledge may also help introduce adequate countermeasures, such as individualized cognitive training interventions tailored specifically to the progressive stage of cognitive decline.

All the future directions described so far suggest that we can improve the current categorial system of cognitive domain by incorporating empirical evidence and information about temporal change within this system. However, the gap between diagnostic guidelines and empirical evidence is not the only threat to the validity and reliability of cognitive diagnostics in PwPD; the operationalization of cognitive functioning as a categorial system with distinct cognitive domains poses challenges itself. Replacing one categorial system with another might improve its utility but overlooks the fundamental problems inherent in such systems. Specifically, categorial systems require definite classifications of cognitive test scores into cognitive domains. However, cognitive tasks used in neuropsychological test batteries typically engage multiple cognitive processes, so observed scores are composed of various conceptual and method variances. A categorial system of cognitive domains ignores this ambiguity, attributing cognitive test score to only one cognitive domain while neglecting the influences of other cognitive processes and task features involved. As an alternative, our findings – along with other findings (Kan et al., 2019) and existing literature on network neuropsychology (Ferguson, 2022) – suggest that modeling cognitive functioning as a complex system operationalized through a network model of cognitive test scores could be a promising alternative. Network models allow the visualization of multivariate conditional associations between cognitive test scores, revealing relationships between cognitive test scores that remain hidden in a definite categorial system. This approach enables both researchers and clinical neuropsychologists to acknowledge such dependencies and interpret cognitive performance accordingly.

However, we are not yet ready to transition from categorial systems toward network models of cognitive functioning. This is because we lack indices to quantify and characterize cognitive performance within such network models. Future studies should further investigate the potential of cognitive network models and aim to develop appropriate, sensitive network indices that can characterize cognitive impairment. One study demonstrated that network indices might be sensitive to cognitive changes that traditional cognitive diagnostics cannot detect. Specifically, they observed a gradient of subtle changes in a network centrality measure across groups of cognitively healthy people, people with SCD, and people with MCI along the dementia risk spectrum (Grunden & Phillips, 2024b). Another study found that network

connectivity in cognitive network models appears to be associated with cognitive performance. The study reported increased connectivity in a group of people with MCI after receiving a cognitive training intervention, positioning network connectivity as a promising marker for cognitive change (Scharfenberg, Kalbe, & Ophey, 2023).

Future studies should specifically focus on the potential of indices derived from idiographic network models (Epskamp, Waldorp, et al., 2018). Such models are estimated from many repeated measurement occasions of the same individual, for example, using intensive longitudinal measurement (Laurenceau et al., 2026). While idiographic network models of cognitive test scores have not yet been described in the literature, several studies in psychopathology have investigated their potential. For example, research has explored idiographic network models for depression (Cusack et al., 2024; Rodriguez et al., 2022) or posttraumatic stress disorder (Bridges-Curry, 2025; Reeves & Fisher, 2020). Idiographic network models of cognitive test scores could significantly advance our understanding of cognitive functioning in PwPD across several domains. First, they could provide individualized insights into the mechanisms underlying cognitive change by modeling the sequential and staged progression of cognitive decline in PwPD. Second, they would enable the linkage of network characteristics from individual networks to traditional quantifications of cognitive performance, with the aim to develop valid and sensitive metrics that characterize cognitive performance and decline within the network framework. Third, by detecting subtle changes in the network system and gaining a deeper understanding of how cognitive decline progresses, there is a potential to develop “early warning systems” of cognitive decline. This concept is already under investigation in psychopathology, where researchers aim to predict depression onset based on idiographic network models from ecological momentary assessment data (Fried et al., 2023). Fourth, after initial suggestions that network models could identify promising intervention targets proved not as straightforward as expected (McNally, 2016; Rodebaugh et al., 2018; Spiller et al., 2020), idiographic network models might still hold this promise (Castro et al., 2023; Castro et al., 2024). In summary, this dissertation project not only makes valuable contributions to refining definitions of cognitive domains but opens the door to a new framework of cognitive diagnostics based on a network perspective on cognitive functioning.

In empirical studies II and III of this dissertation project, network models consisted solely of cognitive test scores, aiming to represent cognitive functioning as accurately as possible. However, network analysis allows the integration of different types of data within a single network model. For example, some network neuropsychology studies include demographic variables – such as age, gender, or education – in addition to cognitive test scores for a more detailed investigation of their influence on cognitive functioning (e.g., Ferguson, 2021; Grunden & Phillips, 2024b; Tosi et al., 2020). Furthermore, network models could be expanded by incorporating other clinically relevant outcomes, such as genetic factors, other motor or non-motor symptoms in PD, digital biomarkers like actigraphy data, or neuroimaging data. This integration would enhance our understanding of the relationships between different data modalities in cognitive decline in PwPD. In particular, combining neuroimaging data with cognitive test scores in a single network model appears promising for uncovering mechanism and progression patterns of cognitive decline in neurodegenerative diseases like PD. Various methodological approaches have been proposed for integrating network models of brain and behaviour (Blanken et al., 2021). In the field of network neuropsychology, one study (currently in preparation for publication but available as a conference abstract) estimated a “bio-cognitive network model”, that is, a network model integrating cognitive, demographic, and neuroanatomical variables (e.g., white matter burden, hippocampal volume) across samples with various cognitive status across the dementia risk spectrum (Grunden & Phillips, 2024a). Similar approaches for samples of PwPD could specifically test hypotheses derived from the DSH of cognitive decline in PwPD.

3.5.2. Implications for clinical practice

Many implications for future research also indirectly inform clinical practice. For instance, research on cognitive domain structures, network metrics for quantifying cognitive performance, and idiographic network models of cognitive functioning have the potential to enhance diagnostic procedures and guidelines used in clinical practice. However, we can also derive direct implications for clinical practice of cognitive diagnostics in PwPD as it is currently employed.

One direct implication from the findings of this dissertation project is to avoid including test scores that are too similar to each other, such as test scores derived from the same test

paradigm or that measure very similar cognitive functions, or to aggregate such scores into a single score. Findings of study II (Scharfenberg et al., 2025) demonstrated that very similar test scores can introduce redundancy into the neuropsychological test battery. Reducing this redundancy by eliminating tests may help interpret results of neuropsychological testing (see the following paragraph) and to reduce burden of neuropsychological testing in PwPD. Notably, this issue is already acknowledged in the MDS diagnostic guidelines for PD-MCI. These guidelines recommend against using two highly similar tests (e.g., two story recall tests) or highly correlated scores from the same test (e.g., immediate and delayed recall of a word list) to meet the criterion of two test scores indicating impairment (Litvan et al., 2012). However, the dissertation project's findings show that test scores can also be highly correlated even when assumed to belong to different cognitive domains (e.g., copying figures and recalling figures). Therefore, the warning should be expanded accordingly for the MDS PD-MCI guidelines. Additionally, drawing from the conceptual replication performed with data from people with healthy cognition in study II, such warnings should also be introduced to the DSM diagnostic guidelines for neurocognitive disorders (American Psychiatric Association, 2013).

As a second clinical implication, we should adapt the DSM approach for defining cognitive domains (American Psychiatric Association, 2013), that is, including descriptive cognitive functions or processes rather than specific cognitive tests. The latter approach is used in the MDS diagnostic guidelines for PD-MCI (Litvan et al., 2012) and was recently updated following the same rationale (Bezdicek et al., 2025; Biundo et al., 2025). However, cognitive tests typically require multiple cognitive functions and processes simultaneously. The empirical subprojects showed that cognitive tests assumed to represent different cognitive domains can still be meaningfully associated due to both, conceptual and method variance. Assigning specific cognitive tests to cognitive domains risks overlooking the involvement of various cognitive processes and task features.

If we retain a categorical system of cognitive domains for cognitive diagnostics, we should a) assign cognitive functions or processes to cognitive domains instead of specific cognitive tests and b) map out task features and all cognitive processes presumably involved in a task, as done in study III (Scharfenberg, Kalbe, Ophey, et al., 2026) and by Steyvers and Schafer (2020). This approach could ensure valid interpretation of cognitive test scores by

considering all relevant task information. Similarly, network models from empirical studies, such as those from study II and III, can help identify and raise awareness about dependencies of different cognitive tasks.

Study III provides clinically relevant longitudinal information about the organization of cognitive functioning, challenging the implicit assumption of temporally stable cognitive domains. Although further research is needed to incorporate longitudinal information into diagnostic guidelines, the findings can still raise awareness of a potential mismatch between cross-sectional cognitive domains and longitudinal cognitive trajectories. Similarly, the findings of network loadings from studies II and III might suggest that some cognitive tests could be useful as informative measures in cross-sectional cognitive diagnostics but not necessarily for monitoring cognitive change longitudinally, such as the digit span tasks that showed appropriate network loadings in cross-sectional study II but very low network loadings in longitudinal study III. However, we recommend not to draw premature conclusions from the first studies on this matter. Future research investigating the informativeness of network loadings for diagnostic accuracy and longitudinal monitoring might provide empirically based recommendations in the future.

In summary, cognitive domain definitions in their current form might challenge validity and reliability of cognitive subtype diagnoses. Reasons include unclear definitions (e.g., defined by cognitive tests versus cognitive functions), neglecting method variance, and not taking into account temporal dynamics of cognitive functioning. Additionally, there is the issue of inconsistent cognitive domain definitions from different diagnostic guidelines which both may be applied to PwPD depending on the context. As explained by the hypothetical case described in chapter 1.3.1., different cognitive domain definitions may result in inconsistent cognitive subtype diagnoses. A recent unpublished work aimed to quantify the extent of this issue, comparing cognitive subtypes derived from MDS versus DSM definitions of cognitive domains in PwPD with PD-MCI from the DEMPARK/LANDSCAPE study, focusing on definitional differences in cognitive domains executive functions, attention, and language. The analysis revealed that only 48.25% of cases showed the same cognitive subtype profile when comparing cognitive domain subtype diagnoses between MDS and DSM criteria (Scharfenberg, Kalbe, Balzer-Geldsetzer, et al., 2026). To avoid this issue, clinical practice needs both, consistent

diagnostic guidelines with cognitive domain definitions based on empirical findings and a commitment of clinical neuropsychologist to adhere to such guidelines.

CHAPTER 4 – GENERAL CONCLUSION

The present thesis project reveals the considerable gap between theoretical assumptions about cognitive domains and empirical findings. Inconsistent definitions of cognitive domains and diagnostic guidelines may affect both the reliability and validity of cognitive diagnoses in PwPD and research aiming to uncover cognitive decline mechanisms and their links to PD-specific biomarkers. Applying psychometric network analysis methods, the empirical studies of this thesis project demonstrate that cognition as a complex system cannot be forced into a rigid categorical concept. Instead, they present network perspectives as a promising alternative to cognitive domain models. In other words, cognitive functioning should be viewed as a complex system, that is, a network model, rather than a modular, categorical system of cognitive domains. Adapting a holistic view in cognitive functioning, network models may represent shared cognitive processes more accurately than categorical systems relying on empirically unfounded reductionism. To integrate the network framework into clinical cognitive diagnostics, further research is needed to develop and establish new measures for cognitive performance based on network models of cognitive test scores. In sum, the present thesis highlights the often-neglected issue of cognitive domains in PwPD to light, raises awareness of its clinical implications, and may lay the groundwork for a new conceptualization of the organization of cognitive functioning in PwPD.

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ORIGINAL PUBLICATIONS

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STUDY I



Scharfenberg, D., Ophey, A., Lessmann, A., Folkerts, A.-K., Kromke, K., Stahl, J. & Kalbe, E. (2026). Understanding cognitive domains in Parkinson's disease: A scoping review of empirical studies. *Neuropsychology Review*. <https://doi.org/10.1007/s11065-025-09691-5>

STUDY II



Scharfenberg, D., Kalbe, E., Balzer-Geldsetzer, M., Berg, D., Hilker-Roggendorf, R., Kassubek, J., Liepelt-Scarfone, I., Mollenhauer, B., Reetz, K., Riedel, O., Roeske, S., Schulz, J.B, Storch, A., Trenkwalder, C., Witt, K., Wittchen, H.-U., Dodel, R. & Ophey, A. (2025). A network perspective on cognition in individuals with Parkinson's disease. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, 17(1), e70091. <https://doi.org/10.1002/dad2.70091>

STUDY III



Scharfenberg, D., Kalbe, E., Ophey, A., Balzer-Geldsetzer, M., Berg, D., Hilker-Roggendorf, R., Kassubek, J., Liepelt-Scarfone, I., Mollenhauer, B., Reetz, K., Riedel, O., Roeske, S., Schulz, J.B, Storch, A., Trenkwalder, C., Witt, K., Dodel, R. & Deserno, M. (2026). Temporal dynamics of cognitive functioning in people with Parkinson's disease. *npj Parkinson's disease*, 12, 86. <https://doi.org/10.1038/s41531-026-01338-3>

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APPENDIX



Understanding Cognitive Domains in Parkinson's Disease: A Scoping Review of Empirical Studies

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Abstract

Cognitive domains (e.g. memory, attention, or executive functions) play a crucial role in cognitive diagnostics. However, cognitive domain definitions and the assignment of cognitive tests to these domains lack both consensus and empirical justification in current guidelines for cognitive diagnostics. Focusing on this issue in Parkinson's disease (PD), this scoping review aims to provide an overview of empirical findings from dimensionality reduction analyses applied to cognitive test scores of individuals with PD. The research addressed three questions: (i) Which methods were used to empirically evaluate cognitive domain differentiations in PD? (ii) Could previously assumed cognitive domains in PD be reproduced by empirical analyses? (iii) Which cognitive domain models did the studies use as its theoretical framework? An a priori defined systematic literature search identified 22 eligible studies published between 1963 and 2022, mainly using exploratory methods such as Principal Component Analysis or Exploratory Factor Analysis to identify a cognitive domain structure in people with PD. These studies were highly heterogeneous in specific methodological configurations of statistical methods, such as rotation and extraction methods. Only few studies referred to the Movement Disorder Society (MDS) guidelines for cognitive diagnostics in PD, and none successfully reproduced previously assumed cognitive domain structures by (exploratory) empirical analysis. The inconsistent results regarding the structure of cognitive functioning might result from heterogeneous samples and methods. Overall, the results challenge the validity and reliability of cognitive diagnoses in PD, highlighting a need for more robust empirical support to improve diagnostic frameworks.

Keywords Cognition · Factor analysis · Parkinson's disease · Cognitive impairment · Dimensionality reduction · Neuropsychological testing

Introduction

Cognitive domains play a crucial role in cognitive diagnostics. For instance, the Diagnostic and Statistical Manual (DSM; American Psychiatric Association, 2013),

categorizes cognitive functions into six cognitive domains, namely attention, executive function, memory and learning, language, visuo-perceptual function, and social cognition. The DSM defines those domains and provides examples of symptoms for each domain and of ways to objectively

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assess each cognitive domain, even though not providing examples of specific neuropsychological tests. Cognitive domains also play a crucial role for cognitive diagnostics in people with Parkinson's disease (PD), the second most prevalent neurodegenerative disease, in whom cognitive decline is a frequent, debilitating non-motor symptom (Aarsland et al., 2021). PD-specific guidelines for cognitive diagnostics, such as the diagnostic criteria for mild cognitive impairment in individuals with PD (PD-MCI) and dementia in individuals with PD (PDD) by the Movement Disorder (MDS) Society Task Force, also rely on the concept of cognitive domains. PD-MCI is defined by gradual cognitive decline and measurable cognitive impairment that does not significantly interfere with functional independence (Litvan et al., 2012). In contrast, PDD is defined by cognitive decline and multiple-domain cognitive impairment which impairs daily life (Emre et al., 2007).

For the comprehensive level II neuropsychological evaluation of PD-MCI, the MDS task force recommends assessing five cognitive domains (attention and working memory, executive function, memory, language, visuospatial function) by applying two cognitive tests associated with each cognitive domain. The criteria include recommendations of specific cognitive tests to assess each cognitive domain. Further, they propose an optional subtype classification based on the number of cognitive domains that are identified as impaired (i.e., single-domain MCI vs. multiple-domain MCI). Another common practice, even though not recommended by the MDS PD-MCI criteria, is to (additionally) differentiate subtypes based on whether memory is impaired or not (i.e., amnesic vs. non-amnesic PD-MCI, Kalbe et al., 2016). The level I diagnostic recommendations for PDD also rely on the concept of cognitive domains and specify that impairment must be prevalent in more than one of four cognitive domains (attention, executive function, visuo-constructive ability, memory), suggesting specific cognitive tests for assessing these cognitive domains (Dubois et al., 2007).

Interestingly, there is no consensus regarding the classification of cognitive domains and the assignment of cognitive tests or functions into these domains for cognitive diagnostics in general. To illustrate, the DSM defines six cognitive domains in its criteria for diagnosing neurocognitive impairment, while the MDS proposes five cognitive domains in its criteria for PD-MCI but four cognitive domains in its criteria for PDD. Furthermore, the DSM and MDS criteria differ regarding to the assignment of cognitive tests (MDS) or functions (DSM) to cognitive domains: The DSM categorizes working memory within the executive function domain, whereas the MDS criteria categorize it within the attention domain. Moreover, the DSM criteria define verbal fluency as a language function, whereas the MDS criteria

define verbal fluency tasks as a measure for executive function. These inconsistencies in assigning cognitive domains is highlighted by empirical findings that yielded contradicting results. For instance, verbal fluency has been variably identified as part of the language domain (Whiteside et al., 2016) or as part of the executive function domain (Aita et al., 2019) in individuals without cognitive impairment. Such definitional ambiguities could potentially compromise the validity and reliability of cognitive diagnoses in individuals with PD, particularly for PD-MCI subtypes that rely on well-defined cognitive domains. To illustrate this issue, assume the following example of an individual showing impairments in one task measuring executive functions (as acknowledged by both diagnostic guidelines) and a verbal fluency task. According to the DSM criteria, the individual presents with multiple domain cognitive impairment in the domains executive functions and language. According to the MDS diagnostic guidelines for PD-MCI, the same individual presents with single-domain impairment in the executive function domain.

Subtype classifications may inform patient counseling and individual disease prognosis: PD-MCI cognitive subtypes are shown to be associated with different patterns of brain changes (Devignes et al., 2022), provide insights into the underlying pathophysiology of PD (Goldman et al., 2018), conversion rates to PDD (Chung et al., 2019; Goldman et al., 2018) or clinical motor symptoms (Amboni et al., 2022) when distinguishing between amnesic and non-amnesic MCI. To date, there is no empirical study showing if and how subtype prevalence and prognostic accuracy change when switching from one diagnostic guideline to another with different cognitive domain definitions. However, Goldman et al. (2018) surmise that the application of the MDS guidelines for PD-MCI may have led to epidemiological shifts in the relative prevalence of single- versus multiple-domain impairment, as reports of multiple-domain impairments increased. This supports the notion that different diagnostic guidelines may lead to different conclusions about the nature of cognitive impairment. In addition, reliable and valid cognitive diagnoses may be of high clinical relevance in the context of personalized cognitive training interventions to enhance cognitive functioning in individuals with PD (Kalbe et al., 2018), as domain-specific impairments can be used as the basis for planning adequate and effective interventions (Bruno et al., 2024).

Despite the high clinical relevance of cognitive domains, neither the DSM nor the MDS empirically justify their definitions of cognitive domains or the assignments of cognitive tests to these domains. To address this issue, dimensionality reduction methods such as exploratory (EFA) and confirmatory factor analyses (CFA), as well as principal component analysis (PCA) could be applied to cognitive test data of

individuals with PD. However, these methods widely vary in their assumptions and configurations (e.g., rotation methods or the method used to define the number of factors to extract in EFA or PCA), which can increase the scope of interpretations. Further, a precise factor determination further depends on characteristics such as sample size, factor correlations or items per factor (Keith et al., 2016).

To the best of our knowledge, no comprehensive review summarized empirical findings on the evaluation of cognitive domains in PD, or other clinical groups, to date. This scoping review aims to fill this gap in the literature by providing an overview of the currently existing empirical attempts to extract factors or dimensions from cognitive test data of individuals with PD. Given the considerable heterogeneity of potential methodologies and the absence of prior review articles on this topic, we consider a scoping review to be the most appropriate approach.

The primary aim is to synthesize empirical evaluations of cognitive domain differentiations and their assigned cognitive tests in individuals with PD. To this end, we aim to address the following research questions:

1. Which methods have been used to empirically evaluate differentiations of cognitive domains and their assigned cognitive tests in individuals with PD?
2. If studies categorized cognitive tests into cognitive domains on a theoretical basis, were they able to reproduce this categorization in their analyses?
3. Did studies refer to the DSM definition of cognitive domains or the MDS criteria on diagnosing PD-MCI?

Methods

For this scoping review, we adhered to the norms and recommendations outlined in the extension of the Preferred Reporting Items for Systematic reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR) checklist (Tricco et al., 2018). The PRISMA-ScR checklist for this scoping review can be found as Supplementary Material 1. We preregistered the protocol for this scoping review on PsychArchives (Scharfenberg et al., 2023) by using the preregistration template for scoping reviews based on the Preregistration for Quantitative Research in Psychology Template (PRP-QUANT) and the PRISMA-ScR (Leibniz Institute for Psychology, 2024).

Search Strategy and Selection Criteria

To address the interdisciplinary nature of this research question, we conducted a systematic literature search in two databases encompassing medical and psychological sources.

Specifically, we searched the databases Ovid MEDLINE, which included published and unpublished sources from 1946 to the present, and PsycInfo, which included sources with no restriction on year of publication (i.e., from 1806 to the present). The search string included terms related to (a) PD, (b) cognition and neuropsychological assessment, and (c) dimensionality reduction methods. We combined search terms from these categories using search string operators to ensure that each potentially eligible source should contain at least one search term from each category. The full search string for both databases is presented in Supplementary Material 2.

We considered sources of English and German language of all study types. To be eligible for the review, the following inclusion criteria were applied:

- must be original research (published or unpublished)
- includes relevant ethical approvals
- conducted a statistical analysis to extract a factor or dimensionality structure of cognitive functions
- use of cognitive test data
- sample of individuals with PD.

The search was conducted on 20 December 2023. The results from both databases were then imported into Endnote, where duplicates were removed. Then, results were imported into Covidence (2023), a web-based collaboration software platform that streamlines the production of systematic and other literature reviews. In Covidence, further duplicates were removed and titles and abstracts were screened for eligibility. Two reviewers (DS, KK) screened the titles and abstracts independently and a third reviewer (EK) resolved any conflicts that arose. After abstract screening, one reviewer (DS) reviewed the scanned full texts for the final eligibility. Then, one reviewer extracted the data of interest from the eligible sources (DS) and a second reviewer (AL) checked all extracted data for correctness.

Data Extraction

The main information of interest included sample size, study participants' cognitive status, statistical methods used for dimensionality reduction, assumed cognitive domain structure, theoretical background of assumed cognitive domain structure, and empirically extracted factors or dimensions (for exploratory dimensionality reduction analyses) or model fit indices values (for confirmatory dimensionality reduction analyses). The preregistered data charting form that had been piloted with one source of evidence prior to submission of the preregistration can be found along with the preregistration of this scoping review on PsychArchives (Scharfenberg et al., 2023). During data extraction,

additional information of interest were included in the data charting form, such as specific information on assessments of verbal fluency tasks. We retained all columns from the preregistered data charting form. The final data charting form containing all variables of interest can be found as Supplementary Material. Finally, we summarized extracted data descriptively according to the research questions. In addition to the preregistered research questions, we also summarized information on studies that assessed verbal fluency tasks which are among the most contentious tasks in terms of their assignments to cognitive domains. We selected verbal fluency tasks because this family of cognitive tests are consistently referred to as verbal fluency tasks, even though different subtasks exist (e.g., phonematic, semantic, action, or alternating verbal fluency). We also summarize descriptive exploratory results on study objectives and the heterogeneity of variables in the sources of evidence.

Following our preregistration, we did not perform a risk of bias analysis, but conducted a critical appraisal of the sources of evidence. This includes assessing the completeness of reporting for our variables of interest and identifying any critical information gaps necessary to validly interpret the published data and results. To this end, we defined four data domains for missing data: i) demographic data including age, gender, and education information of the sample, ii) cognitive status data including cognitive status information and cognitive screening test scores, iii) information on PD characteristics including Hoehn & Yahr stages (Hoehn & Yahr, 1967), Unified Parkinson's disease rating scale part III (UPDRS-III) scores (Fahn, 1987), disease duration, Levodopa equivalent daily dose (LEDD), and iv) information on employed dimensionality reduction methods. We judged the missingness of data as “low” if none of the information of interest in a data domain were missing, “some” if some of the information were missing, and “high” if all of the information of interest in a data domain were missing. We describe the critical appraisal of missing information in the exploratory results section.

Data Synthesis

Given the scoping review approach, we only analyzed the extracted data descriptively. We did not conduct quantitative statistical models of the extracted data or pursued meta-analytic approaches.

Results

The systematic literature search initially identified 900 references as potentially eligible for inclusion in the review. After removing duplicates using EndNote, Covidence, and

manual checks, we screened a total of 705 abstracts. Of these, we excluded 653 sources. Of the 52 remaining studies, we failed to retrieve one study from year 1970 that also provided no author contact information. Thus, 51 studies were assessed for eligibility and 22 studies were ultimately included in the review. More detailed information about the search and selection process are presented in Fig. 1. Table 1 provides a comprehensive summary of all relevant information related to our research questions for the 22 studies included in this review.

Research Question 1: Methods Used to Empirically Evaluate Differentiations of Cognitive Domains

We categorized dimensionality reduction methods into exploratory vs. confirmatory methods (see Fig. 2). Of 22 studies, one performed confirmatory analyses to determine a factor or dimensionality structure of cognitive test scores, while 17 studies performed exploratory analyses and four studies used both approaches. Confirmatory analyses were exclusively performed as CFA ($n=5$ studies). Exploratory analyses were based on EFA ($n=3$), PCA ($n=14$), Thurstone centroid FA (TCFA, $n=1$), exploratory structural equation modelling (ESEM, $n=1$), or provided insufficient analysis information ($n=1$). An overview and short description of each method used in the sources of evidence is presented in Supplementary Material 3. Of the 19 studies that used EFA, TCFA and PCA, 14 used the varimax orthogonal rotation method and five studies used oblique rotation (specifically, two studies used oblimin rotation, one study used promax rotation and two studies did not specify the rotation method). The number of factors or components to be extracted in these studies was determined using the Kaiser-Guttman rule (i.e., extracting all factors or components with eigenvalues > 1 ; $n=7$), scree-plot ($n=2$), a combination of Kaiser-Guttman rule and scree plot ($n=1$), retaining factors with eigenvalues > 0.5 ($n=1$), and model fit indices χ^2 , (standardized) root mean square residual (SRMR, RMR), root mean square error of approximation (RMSEA) and percentage of common variance accounted for by a single factor ($n=1$). Eight studies did not report details on how they decided on the number of factors to extract.

Research Question 2: Reproduction of Assumed Cognitive Domains

Of the five studies that performed CFA, four reported corresponding model fit indices, specifically Comparative Fit Index (CFI, $n=4$), Tucker-Lewis Index (TLI, $n=4$), RMSEA ($n=4$), χ^2 ($n=3$), SRMR ($n=3$), and RMR ($n=1$). These four studies performed a total of 17 CFAs. None of the analysis resulted in a good model fit across all reported indices

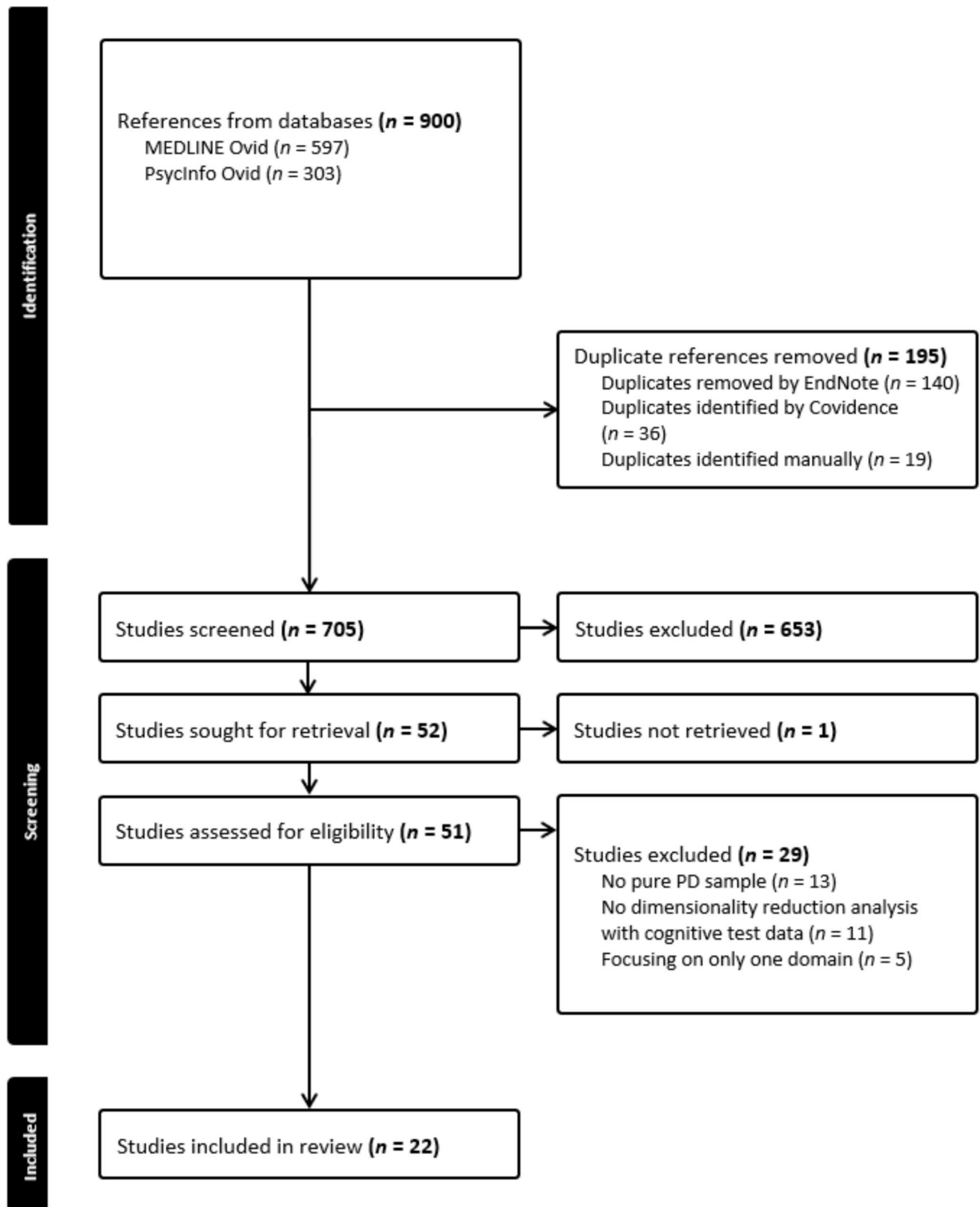


Fig. 1 Flowchart of search and selection process. Note. PD=Parkinson's disease

Table 1 Overview of sources of evidence included with information regarding main research questions

Study	Sample size(s)	Cognitive status	Statistical method	Assumed domain model	Domains replicated?
Benge et al. (2017)	N=357	Mixed (75% PD-NC, 21% PD-MCI, 1.4% PDD)	EFA with Promax oblique rotation and Kaiser-Guttman rule	No assumption	NA
Cholerton et al. (2014)	N=95	PD-MCI	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	MDS	no
Chung et al. (2021)	N=257	Without dementia	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	NA	no
Chung et al. (2020)	N=350	Mixed („nondemented“, n=142 with PD-MCI)	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	NA	no
Clavijo-Moran et al. (2022)	N=100	NA	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	Neural correlates	no
Connolly et al. (2020)	N=100	NA	CFA	Previous EFA solution	NA (CFA)
	N=288	NA	CFA (5)	Previous study; Cattell-Horn-Carroll (3); Spearman's g-factor of intelligence	NA (CFA)
Dujardin et al. (2004)	N=288	NA	ESEM (4)	No assumption	NA
	N=44	Without dementia	PCA	NA	no
	N=33	NA	PCA with varimax orthogonal rotation	No assumption	NA
Hardyck and Petrinovich (1963)					
Johnson and Galvin (2011)	N=71	PDD	CFA	NA	NA (CFA)
Lawson et al. (2016)	N=47	Without dementia	CFA	NA	NA (CFA)
	N=66	Mixed (n=39 PD-NC, n=18 PD-MCI, n=9 PDD)	PCA with oblimin oblique rotation	MDS	no
Lawson et al. (2016)	N=219	Mixed (n=173 PD-NC, n=46 PD-MCI)	PCA with oblimin oblique rotation	MDS	no
Levita and Riklan (1965)	N=24	NA	Thurstone centroid factor analysis with varimax orthogonal rotation	No assumption	NA
	N=26	NA	Thurstone centroid factor analysis with varimax orthogonal rotation	No assumption	NA
Levita and Riklan (1967)	N=21	NA	PCA with varimax orthogonal rotation	No assumption	NA
Liepelt-Scarfone et al. (2012)	NA (2)	NA	PCA with varimax orthogonal rotation	No assumption	NA
	N=121	Mixed (19.8% PDD, all participants: MMSE < 18)	EFA with oblique rotation, Kaiser-Guttman rule and scree-plot	MDS	no
Shirzadi et al. (2018)	N=81	NA	Unclear (Factor Analysis with scree-test)	No assumption	NA
Smith et al. (2020)	N=1738	Without dementia	CFA (4)	Previous studies (4)	NA (CFA)
	N=797	PD-MCI	CFA (4)	Previous studies (4)	NA (CFA)
	N=157	PD-MCI	CFA (4)	Previous studies (4)	NA (CFA)
	N=856	Without dementia	EFA with oblique rotation (2), scree plot (1)/constrained to 3 factors	MoCA domain structure; previous study	no
	N=882	Without dementia	CFA (2)	Previous EFA solution (2)	NA (CFA)
Specketer et al. (2019)	N=197	Without dementia	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	No assumption	NA
Stegemöller et al. (2014)	N=35	NA	PCA with varimax orthogonal rotation	No assumption	NA
Verleden et al. (2007)	N=100	NA	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	No assumption	NA

Table 1 (continued)

Study	Sample size(s)	Cognitive status	Statistical method	Assumed domain model	Domains replicated?
Weintraub et al. (2011)	<i>N</i> =513	PDD	PCA with varimax orthogonal rotation and eigenvalues>0.5	No assumption	<i>NA</i>
Yang et al. (2009)	<i>N</i> =383	<i>NA</i>	CFA (2); EFA with varimax orthogonal rotation and extraction by model fit indices (2)	RBANS domain structure (3); previous EFA solution	<i>NA</i> (CFA) no
	<i>N</i> =215	<i>NA</i>	CFA (2)	RBANS domain structure; previous EFA solution	<i>NA</i> (CFA)
Zgaljardic (2004)	<i>N</i> =32	Without dementia	PCA with varimax orthogonal rotation	Theoretical associations with brain circuits	no

Numbers in parenthesis refer to the number of analyses performed with the indicated specification. Replicated domains refer to exploratory analyses. PD-NC=individuals with Parkinson's disease and normal cognition. PD-MCI=individuals with Parkinson's disease and mild cognitive impairment. PDD=individuals with Parkinson's disease dementia. EFA=Exploratory Factor Analysis. PCA=Principal Component Analysis. CFA=Confirmatory Factor Analysis. ESEM=Exploratory Structural Equation Modelling. MDS=Movement Disorder Society task force diagnostic criteria for mild cognitive impairment in Parkinson's disease. MoCA=Montréal Cognitive Assessment. RBANS=Repeatable Battery for the Assessment of Neuropsychological Status.

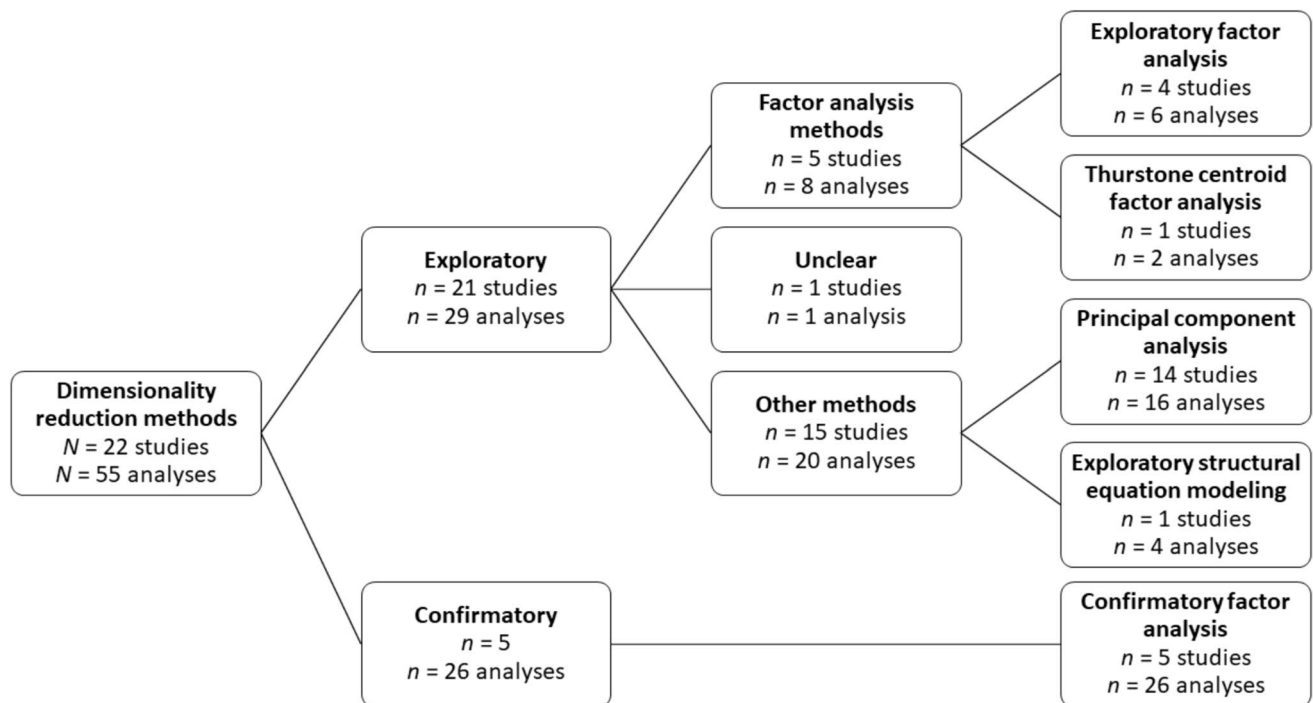


Fig. 2 Overview of dimensionality reduction methods used in eligible sources of evidence. Please note that some studies applied more than one analysis with different methods (e.g. exploratory as well as con-

firmatory approaches), thus exceeding *N*=22 in sum. *N*=number of studies that applied the indicated analysis

according to widely accepted cut-offs for good model fit (Byrne, 1994). However, eleven analyses reported good model fit for at least one of the reported indices, namely CFI (*n*=7), TLI (*n*=7), SRMR (*n*=7), and χ^2 (*n*=1). For six analyses, none of the reported model fit indices indicated a good model fit.

Of the 21 studies that performed exploratory analyses, eleven assumed prior assignments of cognitive tests to cognitive domains. The number of assumed domains

ranged from 1 to 6, and some using a hierarchical approach assuming a global cognition domain in addition to five or six cognitive domains. The related analysis results then indicated two (*n*=3), three (*n*=9), four (*n*=7), six (*n*=2), or seven (*n*=1) empirical domains (*NA*=1). Table 2 provides an overview of analyses that assumed domains prior to analysis and the identified domains labels post-analysis. In the nine analyses presented in Table 2, a total of 26 cognitive domains were identified and distinctively

Table 2 Overview of studies that assumed cognitive domains prior to analysis and named identified domains after analysis

Empirically identified cognitive domains																				
Study	Sample	Method	Assumed domains	Attention/Processing Speed	Fluency/Visuospatial	Contextual/Declarative Memory	Working Memory/Executive	List-learning/declarative memory	Construction	Language	Visual memory/spatial function	Frontal/working memory/ function	Attention/working memory/ function	Non-mnemonic	Memory/Executive function	Global cognition	Word-list memory/recall	Praxis & perceptual-motor ability	Executive function	Memory/learning & information with semantic memory
Cholerton et al. (2014)	N=95 with PD-MCI	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	Learning & memory Executive Attention/working memory Language Visuospatial Global cognitive function	X	X	X	X	X	X	X	X	X	X							
Chung et al. (2021)	N=257 without dementia	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	Attention & working memory Language Visuo-spatial function Verbal memory Visual memory Frontal/executive function								X	X	X	X						
Chung et al. (2020)	N=350 mixed sample („non-demented“, n=142 with PD-MCI)	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	Attention & working memory Language Visuo-spatial function Verbal memory Visual memory Frontal/executive function								X	X	X	X						
Clavijo-Moran et al. (2022)	N=100	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	Cortical Subcortical											X	X					
Lawson et al. (2016)	N=66 mixed sample (n=39 PD-NC, n=18 PD-MCI, n=9 PDD)	PCA with oblique rotation	Attention Memory Executive function Visuospatial function Language Global cognitive function											X	X	X				

Table 2 (continued)

Empirically identified cognitive domains																								
Study	Sample	Method	Assumed domains	Attention/ Process- ing Speed	Fluency/ Visuospatial	Contextual/ Declarative Memory	Working Memory/ Executive	List- learn- ing	Con- Lan- struc- tion	Visual Ver- ory/ mem- ory/ func- tion	Frontal/ Atten- tion/ work- ing mem- ory/ lan- guage	Non- mne- sic	Atten- tion	Mem- ory/ func- tion	Global Fron- tal func- tion	Word- list mem- ory & recall	Logi- cal mem- ory & percep- tion	Praxis & visu- al func- tion	Flu- ency & nam- ing abil- ity	Exec- utive func- tion	Mem- ory	Ver- bal atten- tion	Ver- bal learn- ing & infor- mation	Mem- ory of verbal
Lawson et al. (2016)	N=219 Mixed sample (n=173 PD-NC, n=46 PD-MCI)	PCA with oblimin oblique rotation	Attention Memory Executive function Visuospatial function Language Global cognitive function			Memory		declarative memory		visuo- ory/ mem- ory/ func- tion														
Liepert-Sar- fone et al. (2012)	N=121 mixed sample (19.8% PDD, all participants: MMSE<18)	EFA with oblique rotation, Kaiser- Guttman rule and scree plot	Attention Executive function Visuospatial function Memory Language										X		X	X	X	X	X					
Smith et al. (2020)	N=856 (without dementia)	EFA with oblique rotation, constrained to 3 factors	Executive function Memory Verbal attention																	X	X	X		
Yang et al. (2009)	N=383	EFA with varimax orthogonal rotation and extraction by model fit indices	Immediate memory Visuospatial/constructural Language Attention Delayed memory + Global cognition																				X	X

PD-NC=individuals with Parkinson's disease and normal cognition. PD-MCI=individuals with Parkinson's disease and mild cognitive impairment. PDD=individuals with Parkinson's disease dementia. EFA=Exploratory Factor Analysis. PCA=Principal Component Analysis

named. Notably, none of the exploratory analyses were able to fully replicate their postulated assignments of cognitive tests to cognitive domains by applying exploratory analyses to cognitive test data from individuals with PD. One exception was the study of Smith et al. (2020), who reported having replicated an assumed general cognitive domain structure based on previous empirical results reported by other researchers. However, Smith et al. excluded three cognitive test scores compared to the previous analyses and a-priori constrained the number of factors to be extracted to three. While the empirically identified factors were named in accordance with the previously assumed cognitive domains, the assignments of cognitive tests to cognitive domains were not fully replicated. Contrary to the assumption, digit spans backwards loaded more strongly onto the verbal attention factor than onto the executive factor.

Given the ongoing debate about the categorization of verbal fluency tasks within cognitive domains, we summarize results of studies that assessed verbal fluency tasks and performed exploratory analyses ($n=10$). This subset allowed us to compare a-priori postulated assignments of verbal fluency tasks to cognitive domains with the empirical results of dimensionality reduction analyses. Prior to analysis, verbal fluency was assumed to represent executive function ($n=4$), executive/processing function ($n=1$), language ($n=1$), a subcortical neural circuit ($n=1$) or the anterior cingulate cortex circuit ($n=1$). Three studies did not assume cognitive domains before analysis. In dimensionality reduction analyses, verbal fluency was found to be associated with factors/components of executive function ($n=1$), fluency/visuospatial function ($n=1$), fluency & naming ability ($n=1$), a non-mnesic domain ($n=1$), a lexical/verbal generation domain ($n=1$), and global cognition ($n=1$), whereas four studies did not name the resulting factors/components. Importantly, none of the studies successfully reproduced their previously assumed cognitive domains for verbal fluency. Instead, the resulting domains showed even greater heterogeneity than previously assumed domains. The detailed information on the results of analyses containing verbal fluency scores are presented in Table 3.

Research Question 3: Cognitive Domain Model

Among the eleven studies that assumed cognitive domain assignment prior to analyses, four followed the MDS criteria, while none referred to the DSM criteria. Other studies assigned cognitive tests to cognitive domains based on the Cattell-Horn-Carroll model ($n=1$), Spearman's g-factor of intelligence ($n=1$), previous EFA results to then confirm in CFA ($n=3$), an established cognitive test (battery) structure

($n=3$), associations with neural mechanisms ($n=2$), empirical findings from another study ($n=2$), or did not provide information on this ($n=2$).

As the MDS criteria are crucial for cognitive assessment of individuals with PD, we identified the four studies that followed the MDS criteria for assigning cognitive variables to cognitive domains and present their findings in Table 4. Notably, none of the studies were able to confirm the cognitive domain structure proposed by the MDS criteria. Instead, results varied considerably in the number of empirically extracted domains, which ranged from three to seven domains with none of the studies identifying a structure consisting of five domains as proposed by the MDS criteria. Two studies (Lawson et al., 2016, 2017) using the same database extracted the same structure and domain labels. Other than that, only the label "attention" has been assigned by different studies.

Exploratory Results

Study Objectives

To estimate how many of the examined studies acknowledged the issue of cognitive domains in neuropsychological diagnostics of individuals with PD, we identified and coded the aims and objectives of each study. Half of the studies ($n=11$) did not explicitly state that their objective was to perform a dimensionality reduction analysis to identify the structure of cognitive functioning in individuals with PD. Instead, they pursued other objectives, such as exploring the association between cognition and motor symptoms in PD, using FA to reduce redundancy of the neuropsychological test scores and create a composite score of cognitive performance (Chung et al., 2021). Details about the stated objectives in each included source of evidence can be found in the digital data charting form as Supplementary Material. The remaining half of the studies ($n=11$) aimed to identify the structure of cognitive functioning in individuals with PD. However, six of these studies were not concerned with a general understanding of the cognitive organization in individuals with PD, but rather aimed to identify the structure of a cognitive test (battery) for psychometric reasons. Consequently, only five studies explicitly sought to identify a general structure of cognitive functioning in individuals with PD. Notably, three of these studies were published in the 1960s (Hardyck & Petrinovich, 1963; Levita & Riklan, 1965, 1967), leaving only two studies that addressed the issue of cognitive domains in neuropsychological diagnostics in individuals with PD in the last 15 years (Liepelt-Scarfone et al., 2012; Specketer et al., 2019).

Heterogeneity of Relevant Variables

As we noticed during the data charting process, we observed considerable heterogeneity regarding cognitive test variables included in dimensionality reduction analyses. The number of cognitive test scores included in the analyses ranged from 5 to 25, with a mean of $M=13.35$ ($SD=5.15$) and a median of 12. Similarly, sample sizes for the analyses showed a broad range, ranging from 21 to 1738 with a mean of $M=279.48$ ($SD=368.43$) and a median of 121. To adequately present practices regarding number of test score and sample size, we computed the means by considering all unique values within studies, so that one study can contribute more than one, but not the same, value.

Critical Appraisal of Sources of Evidence

Instead of conducting a risk of bias assessment, we assessed and described missing information about the studies' samples or methods. Only one study (Liepelt-Scarfone et al., 2012) provided all information of interest in all four data domains defined for the critical appraisal of missing information (demographic data, information on cognitive status, PD characteristics, and information on the employed dimensionality reduction methods). Five other studies showed overall low levels of missing information too, as information of interest were only missing in one of the data domains. Seven of the 22 included studies showed a high overall level of missing data, whereas the remaining nine studies showed some data missingness. We visualize the critical appraisal in Fig. 3A. Rates of missing data in the included sources of evidence were highest for information on the samples' cognitive status and PD characteristics. Demographic information and information on the dimensionality reduction method employed in the sources of evidence were complete in 14 out of 22 studies (63.63%). A summary of missing information separated into data domains is presented in Fig. 3B. The digital data charting form (Supplementary Material) contains detailed information of missing information of interest on analysis level.

Discussion

Precise diagnostics of cognitive impairment in individuals with PD is an important aspect for individually adapted therapeutic approaches and requires a fundamental understanding of the conceptual structure of these cognitive functions and their relationship. However, currently proposed cognitive domain structures lack consensus and empirical justifications. Thus, this scoping review based on a systematic literature search aimed to provide an overview of empirical

evaluations of cognitive domain differentiations and cognitive tests in individuals with PD. Reviewing findings from 22 studies meeting the review's inclusion criteria, we found that the majority of studies used exploratory dimensionality reduction approaches, with considerable heterogeneity in method specifications. The most frequently employed method was PCA. Interestingly, none of the exploratory analyses were able to reproduce previously assumed assignments of cognitive test scores to cognitive domains. While some CFA results indicated at least partial support for proposed cognitive domain models, they failed to consistently confirm a proposed cognitive domain model empirically. Only four out of 22 studies assigned cognitive functions or test scores to cognitive domains in accordance with the MDS criteria, and none referred to the DSM criteria. The sources of evidence included in this review were highly heterogeneous in terms of both, cognitive test variables and sample sizes included in the analyses. Furthermore, many of the included studies showed missingness of information of interest, especially regarding information on the samples' cognitive status and PD-specific characteristics.

Methods Used to Empirically Evaluate Differentiations of Cognitive Domains

For our first research question, we aimed to identify which methods have been used to empirically evaluate differentiations of cognitive domains and their assigned cognitive tests. We found that the dimensionality reduction methods used within the sources of evidence could be described as both, heterogeneous as well as homogeneous at the same time. On the one hand, the considerable heterogeneity resulted from methodological specifics, such as rotation and extraction methods. This diversity of method specification challenges approaches to summarize and to compare results across studies, as well as to conduct further both quantitative and qualitative analysis of their results required in systematic reviews and meta-analysis.

On the other hand, the methods could also be described to be relatively homogeneous, as the majority of studies employed traditional and established techniques such as EFA, PCA, and CFA. Numerous alternative methods exist that could be used for such analyses in this context, including other PCA-based methods such as parallel analysis (Horn, 1965) and the minimum average partial criterion (MAP, Velicer, 1976), or the maximum likelihood method for factor extraction within EFA (Hayashi et al., 2007).

Additionally, the employed methods in the included studies might not be the most appropriate methods for dimensionality reduction of cognitive test scores. The majority of studies used varimax orthogonal rotation, if a rotation technique was applied. Orthogonal rotation

Table 3 Overview of studies that assessed verbal fluency tasks

Study	Sample size	Cognitive status	Method	Verbal fluency type	Assumed fluency factor	Other cognitive tests in assumed domain	Verbal fluency factor	Other cognitive tests assigned to this factor
Benge et al. (2017)	N=357	Mixed (75% PD-NC, 21% PD-MCI, 1.4% PDD)	EFA with Promax oblique rotation and Kaiser-Guttman rule	Phonemic verbal fluency	NA	NA	Executive Function	Clock Drawing Cube Copy Digit Span Backward Subtractions
Cholerton et al. (2014)	N=95	PD-MCI	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	Phonemic verbal fluency, semantic verbal fluency	Executive function (phonemic fluency) Language (semantic fluency)	Clock Drawing Test (phonemic fluency) Boston Naming Test (semantic fluency)	Fluency/Visuospatial	Benton Judgement of Line Orientation
Clavijo-Moran et al. (2022)	N=100	Not reported	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	Verbal action fluency, alternating verbal fluency	Subcortical	Clock Drawing Sustained Attention Verbal Memory Delayed Verbal Memory Immediate Working Memory	Non-Mnesic	Alternating Fluency Clock Copy Clock Drawing Naming Sustained Attention Working Memory
Dujardin et al. (2004)	N=44	Without dementia	PCA	Alternating verbal fluency, phonemic verbal fluency	Executive Function	Stroop Trial 1 Stroop Trial 2 Stroop Interference Index	NA	Digit Span Backward
Lawson et al. (2016)	N=66	Mixed (NC: n=39, PD-MCI: n=18, PDD: n=9)	PCA with oblimin oblique rotation	Phonemic verbal fluency, semantic verbal fluency	Executive Function	One Touch Stocking	Global Cognition Factor	Mini Mental State Examination Montréal Cognitive Assessment
Liepert-Scarfone et al. (2012)	N=121	Mixed (19.8% PDD, all participants: MMSE < 18)	EFA with oblique rotation, Kaiser-Guttman rule and corresponding scree-plot	Semantic verbal fluency	Executive Function	Digit Span Backward Digit Span Forward Tower of London Trail Making Test A & B	Fluency & Naming Ability	Boston Naming Test Trail Making Test A
Shirzadi et al. (2018)	N=81	Not reported	NA	Semantic verbal fluency	NA	NA	NA	Benton Judgement of Line Orientation Hopkins Verbal Learning Acquisition Trials Letter Number Sequencing Symbol Digit Test

Table 3 (continued)

Study	Sample size	Cognitive status	Method	Verbal fluency type	Assumed fluency factor	Other cognitive tests in assumed domain	Verbal fluency factor	Other cognitive tests assigned to this factor
Speck-eter et al. (2019)	N=197	Not reported	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	Phonemic verbal fluency, semantic verbal fluency	Executive/Processing	Digit Symbol Stroop Color Stroop Color-Word Stroop Word Trail Making Test A	NA	NA
Verleden et al. (2007)	N=100	Not reported	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	Phonemic verbal fluency	NA	NA	NA	Stroop Coloured Wort Test Selective Attention
Zgal-jardic (2004)	N=32	Without dementia	PCA with varimax orthogonal rotation	Letter Fluency Category Fluency Switching Fluency Switching Fluency Accuracy Verbal Fluency Initiation	Anterior Cingulate Cortex (ACC) Brain Circuit	Stroop Color-Word Frontal System Behavioral Scale—Apathy	Lexical/Verbal Generation Factor	

PD-NC=individuals with Parkinson's disease and normal cognition. PD-MCI=individuals with Parkinson's disease and mild cognitive impairment. PDD=individuals with Parkinson's disease dementia. EFA=Exploratory Factor Analysis. PCA=Principal Component Analysis

methods imply an independency of the resulting factors or components, which is, both theoretically and empirically, not reasonable for cognitive test data (van der Maas et al., 2006). Indeed, Costello and Osborne (2005) advise to use oblique rotation over orthogonal rotation because of this very reason. They suggest that oblique rotation leads to more accurate and reproducible results for correlated factors, while results would be very similar to those of analyses with orthogonal rotation, if the factors were truly uncorrelated.

Furthermore, the majority of studies applied exploratory methods such as PCA or EFA. PCA is not a factor analysis method and hence is not appropriate to use for extracting latent factors such as cognitive domains but is rather suited for data reduction purposes (Costello & Osborne, 2005). As EFA and, in particular, PCA do not separate model-variance from residual variance, results of these exploratory methods are heavily influenced by sample specific variance (Floyd & Widaman, 1995), causing the resulting factor models not to be replicable, as has been shown in a simulation study (Keith et al., 2016). This simulation study has also demonstrated that CFA is one of the most accurate techniques for identifying the true number

of factors in intelligence-like data by assessing and comparing model fit of varying postulated models (Keith et al., 2016). Importantly, common guidelines recommend not to use EFA or PCA if a factor structure can already be derived theoretically or from previous empirical findings and tested by CFA (Costello & Osborne, 2005; Henson & Roberts, 2006). Despite these recommendations, CFA has only been applied in five out of 22 studies included in the present review, while EFA and PCA have been applied in 18 studies. However, all of the five studies that have applied CFA were published since 2009, potentially indicating an increased awareness of such guidelines regarding the use of FA, although misconceptions and inadequate usage of these methods still persist up until today. To conclude, further empirical research on cognitive domain structures should primarily include CFA, and compare different cognitive domain structures derived from both, theoretical considerations and empirical findings. Additionally, other dimensionality reduction methods have emerged in recent years, which do not rely on the concept of latent factors but perform dimensionality analysis based on psychometric network models. We discuss possible applications of these innovative methods below.

Table 4 Overview of studies that assigned cognitive tests to cognitive domains according to MDS criteria

Study	Sample	Method	Assumed Domain names	Number of test scores	Number of domains extracted	Extracted domain names
Cholerton et al. (2014)	N=95 with PD-MCI	PCA with varimax orthogonal rotation and Kaiser-Guttman rule	Learning & memory Executive Attention/working memory Language Visuospatial Global cognitive function	17	7	Attention/Processing Speed Fluency/Visuospatial Contextual Declarative Memory Working Memory/ Executive List-Learning Declarative Memory Construction Language
Lawson et al. (2016)	N=66 mixed sample (n=39 PD-NC, n=18 PD-MCI, n=9 PDD)	PCA with oblique oblimin rotation	Attention Memory Executive function Visuospatial function Language Global cognitive function	10	3	Attention Memory/executive function Global cognition
Lawson et al. (2016)	N=219 Mixed sample (n=173 PD-NC, n=46 PD-MCI)	PCA with oblique oblimin rotation	Attention Memory Executive function Visuospatial function Language Global cognitive function	10	3	Attention Memory/executive function Global cognition
Liepelt-Scarfone et al. (2012)	N=121 mixed sample (n=24 PDD)	EFA with oblique rotation and Kaiser-Guttman rule + scree plot	Attention Executive function Visuospatial function Memory Language	19	6	Frontal lobe function Word-list memory and recall Attention Logical memory Praxis & visual perception Fluency & naming ability

PD-NC=individuals with Parkinson's disease and normal cognition. PD-MCI=individuals with Parkinson's disease and mild cognitive impairment. PDD=individuals with Parkinson's disease dementia. EFA=Exploratory Factor Analysis. PCA=Principal Component Analysis.

Confirmation of Assumed Cognitive Domains

The second research question addressed in this review was whether studies were able to reproduce previously assumed categorizations of cognitive tests into cognitive domains. Notably, no study fully achieved this goal. Furthermore, results showed considerable heterogeneity in the number and labels of the extracted dimensions, with 26 distinctively named dimensions identified across nine analyses. These findings have profound implications for clinical practice in cognitive diagnostics in individuals with PD, raising concerns about the validity and reliability of the current approaches. An important issue is the variability of cognitive domain conceptualizations. For example, test scores measuring verbal fluency function have been assigned to various cognitive domains, including executive function, executive/processing function, anterior cingulate cortex brain circuit, subcortical domain, and language. As a result, the same verbal fluency test score of the same individual can be interpreted as impairment in different cognitive domains by clinicians or researchers relying in different cognitive domain definitions. In this case, the identical test result can

lead to diagnoses of either multiple-domain PD-MCI or single-domain PD-MCI, potentially resulting in inadequate planning of individual cognitive rehabilitation using cognitive trainings. Notably, the lack of conceptual consensus undermines the reliability of diagnoses, especially in terms of cognitive subtype classifications. These classifications are assumed to be associated with different rates of cognitive decline and conversion to PDD (Chung et al., 2019) as well as with motor symptoms like gait patterns (Amboni et al., 2022).

One potential solution for the reduced reliability due to differing cognitive domain definitions could be to introduce binding guidelines for cognitive diagnostics, which define cognitive domains and categorize cognitive tests and functions into those domains, and to consequently apply them in both, clinical and research contexts. If necessary, such diagnostic guidelines should ideally be disease-specific if the cognitive domain organization differs between clinical groups. However, it is important to note that differences in the cognitive domain organization cannot simply be identified by empirical results of EFA or PCA that showed different factor solutions for different groups. One remarkably

Fig. 3 Critical appraisal of missingness of information (A) for each of the included sources of evidence and (B) summarized per data domain. Missingness of data was judged as “high” if all information of interest in a data domain was missing, judged as “some” if some of the information were missing and “low” if information were completely reported within a data domain. Visualization created using *robvis* (McGuinness & Higgins, 2021). UPDRS-III=Unified Parkinson’s disease rating scale part III. LEDD=Levodopa equivalent daily dose



example of this misunderstanding is the work of Delis et al. (2003) who found different factor structures when applying PCA to clinical, normative, and mixed samples, concluding that these findings reflect different cognitive organizations in different clinical groups. In fact, instable results of EFA or PCA could be explained by several reasons, such as unrepresentative sampling or unreliable scores (Bowden, 2004). Before assuming that every clinical group has different cognitive organizations, the factor analytic results should be tested on measurement invariance (MI), which refers to the equivalency of latent variables measured across groups. MI in the context of factor analyses, i.e., factorial invariance, can be tested by employing multiple-group CFA (Dimitrov, 2010). Testing for MI ensures not to draw unwarranted

conclusions based on error-prone exploratory methods like EFA and PCA about the instability of factorial structures between different groups.

Application of Existing Guidelines for Cognitive Diagnostics

The MDS criteria addresses some of the above-mentioned challenges, providing a PD-specific cognitive domain structure. To explore this further, our third research question was designed to estimate how widely the PD-specific MDS criteria (or DSM criteria for general cognitive diagnostics) actually have been applied in the sources of evidence. Only four out of 22 studies referred to the MDS PD-MCI criteria

and none to the DSM criteria. Studies employing MDS criteria showed similar heterogeneity of dimensionality reduction analysis results as those employing other frameworks. Thus, the findings do not support a better empirical fit of the MDS criteria compared to other cognitive domain structures. Moreover, no other consistent pattern of results was observed that would emerge as a potential alternative cognitive domain structure. Notably, this issue is not limited to MDS criteria or PD-specific cognitive diagnostics, but also applies to other cognitive diagnostics criteria and clinical groups. For instance, the DSM criteria for neurocognitive disorders (American Psychiatric Association, 2013) also provide no empirical justification for their assignment of specific cognitive functions or tests to cognitive domains.

Future studies should employ CFA for comparing different cognitive domain models of interest and assessing measurement invariance in different samples. Such conceptually guided analyses should ideally include a variety of proposed cognitive domain definitions from different diagnostic guidelines as well as other theories of cognitive functioning, such as the Cattell-Horn-Carroll (CHC) model of intelligence (Jewsbury et al., 2017). The CHC model was developed in the context of intelligence research and is rather a family of models which have evolved over time (Schneider & McGrew, 2018). One CHC model for clinical assessment assumes nine latent factors, namely processing speed, long-term memory encoding and retrieval, working memory, visuospatial ability, fluid reasoning, quantitative ability, auditory ability, and even word fluency as a separate factor. A comprehensive meta-factor analysis of data from over 60,000 cognitively healthy individuals across 52 studies following this approach failed to replicate the DSM cognitive domain structure and found the CHC model to show the best model fit among the tested models (Agelink van Rentergem et al., 2020). Accordingly, future studies should assess measurement invariance of the CHC model in different populations such as people with PD across different cognitive status. Despite these inconsistencies, the cognitive domains as employed in the DSM or MDS criteria are continued to be widely used, without adjustments being made to account for conflicting empirical findings. Consequently, this challenges the validity and reliability of cognitive diagnostics and, ultimately, the foundational concept of cognitive domains itself.

Importantly, our critique is not directed at the cognitive tests themselves, which are essential to assess cognitive functions, but rather specifically at the concept of cognitive domains and the interpretation of cognitive functions within this framework. Labelling cognitive domains and definitely categorizing cognitive test scores (or functions) into cognitive domains leads to a form of reductionism that overlooks the impossibility of measuring isolated cognitive

functions with cognitive tests and neglects the interdependence between cognitive test scores due to overlaps in involved cognitive functions or common variance elicited by the same stimuli or methodology (method variance; Larabee, 2003). This issue gets further complicated by different semantics and categorizations of cognitive domains as well as inconsistent empirical results due to heterogeneous cognitive test batteries, heterogeneous samples with different cognitive status, and applying error-prone exploratory dimensionality reduction methods like EFA and PCA.

However, the concept of cognitive domains is not the only one in cognitive and clinical neuroscience to be affected by such definitional issues. Other examples are the debate about the dementia nomenclature (Petersen et al., 2023) or the Research Domain Criteria Project (RDoC) which aims to develop new ways of classifying mental disorders based on dimensions of observable behavior and neurobiological measures (Sanislow et al., 2010). A common issue for all of these examples seems to be that classic categorial systems to define these constructs cannot adequately capture the heterogeneity and complexity of, e.g., cognitive functions. Therefore, new approaches have emerged in the last years, such as the RDoC project that adopts dimensional conceptualizations of specified functional dimensions of behavior or the network perspective on complex systems that can be applied to a variety of concepts such as mental disorders (Borsboom, 2017) and cognition (Ferguson, 2022; van der Maas et al., 2006).

Network Perspective On Cognition As an Alternative Concept

Challenging the underlying traditional concept of cognitive domains, network theories and network analysis methods applied to cognitive test scores – referred to as network neuropsychology – offer a more holistic perspective on cognition by conceptualizing cognition as a complex interplay of interconnected cognitive functions (Ferguson, 2022). Within the network analysis framework, new methods for dimensionality analysis similar to FA have been developed, such as Exploratory Graph Analysis (EGA; Golino & Epskamp, 2017). EGA shows comparable or even higher accuracy in identifying the number of dimensions when compared to other established methods (Golino et al., 2020). Importantly, although the accuracy of EGA showed to be higher than PCA or EFA in a simulation study, the value of this emerging method has to be determined in the future and based on the appropriate use and interpretation of the EGA in the context of neuropsychological research. Inadequate usage of EGA, as it happened with EFA or PCA techniques, will limit the value of EGA. While EGA could contribute to forming new hypotheses about the cognitive

domain organization in the light of a network perspective of cognition, CFA should still be considered to confirm these hypotheses and ensure measurement invariance of its findings. The EGA framework has good prerequisites for this kind of integrated approach, as its software comes with an integrated CFA option and bootstrapping stability analysis option (Golino & Christensen, 2025) and options for testing measurement invariance via permutation testing (Jamison et al., 2024).

EGA allows to combine both, taking a network perspective and applying dimensionality analysis to identify clusters of cognitive test scores within the network. Applying such new and innovative methods and perspectives could enrich future discussions about the structure of cognitive functioning and facilitate the development of more appropriate cognitive test batteries and diagnostic criteria. One recently published study applying EGA to cognitive test data of individuals with PD found support for the notion to view cognition as an interconnected network of cognitive functions rather than applying a latent factor structure resulting in modular cognitive domains (Scharfenberg et al., 2025). This study was accepted after the end of the systematic literature search, which is why it was not included in the review as a source of evidence. Even though the network analysis methods seem promising to generate valuable insights in the organization of cognitive functioning in future studies, at present, there are neither cognitive diagnostic criteria nor appropriate and established cognitive markers derived from the network perspective framework yet. Therefore, for now, we recommend to be aware of the limitations on the (diagnostic) interpretation associated with assumptions of cognitive domains and empirical evaluations using dimensionality reduction methods. To improve our understanding of how cognitive functions are organized, we also encourage performing more empirical studies on this topic by applying both, traditional and innovative dimensionality reduction methods in combination with CFA and testing measurement invariance.

Limitations and Strengths

The objective of this study was to provide an overview of the empirical research that has been conducted on evaluations of cognitive domains in individuals with PD. We deemed a scoping review the most appropriate form of evidence synthesis, as we did not intend to aggregate our findings to answer a specific question to inform clinical practice (Munn et al., 2018). Instead, we were interested in mapping out the literature and the methodological approaches of the included studies. Our study's results confirmed this approach to be adequate, because sources of evidence showed considerable

heterogeneity in the (statistical) methods applied, such as sample characteristics (e.g. cognitive status, other clinical characteristics) and the (number of) cognitive test scores included in analyses. Thus, a systematic review with the goal to address a specific research question and provide a synthesis of results would have been neither appropriate nor feasible (Munn et al., 2018). Further, although a scoping review can serve as a precursor for a systematic review, this possibility seems unfeasible in light of the considerable heterogeneity between studies observed in this scoping review. The issue of heterogeneous methods could potentially be circumvented by applying meta-factor analysis methods to pooled correlation matrices or individual participant data, as demonstrated in a comprehensive meta-factor analysis of cognitive functioning in cognitively healthy individuals (Agelink van Rentergem et al., 2020). However, the heterogeneity of sample characteristics, including the cognitive status of the included individuals and the varying cognitive test batteries applied in the studies, would complicate applying this approach.

This scoping review stands out from narrative literature reviews by applying an a priori defined systematic literature search (Munn et al., 2018). To ensure comprehensive coverage of the literature, we included search terms related to PD, cognitive diagnostics, and dimensionality reduction methods ensuring to include a wide body of literature. Additionally, we searched two large databases covering medical as well as psychological records, to consider the interdisciplinary nature of the research question at the interface of (neurological) medicine and (neuro)psychology. However, based on the relatively low number of initially retrieved sources compared to other systematic literature searches we cannot fully rule out that we missed sources by our search strategy. Then again, our results showed that few studies explicitly addressed the issue of cognitive domains, suggesting that it is an understudied issue.

Conclusion

This scoping review highlights that, although the concept of cognitive domains is central to the cognitive diagnostics of individuals with PD, there is a notable lack of empirical evidence to support the justification of cognitive domains based on dimensionality reduction results applied to cognitive test scores of individuals with PD. Summarizing findings of eligible studies is hampered by the heterogeneity observed in both, statistical methods employed and clinical characteristics of the PD samples. Overall, the inconsistent findings of the studies included in this scoping review did not support the assumptions about cognitive domains as employed by the MDS guidelines for cognitive

diagnostics in PD-MCI and PDD. Hence, the results challenge the validity and reliability of cognitive diagnoses in individuals with PD, underscoring the need for further research systematically addressing the issue of cognitive domains.

Authors' Contributions

Conceptualization: DS, AO, JS, EK; Data curation: DS, AKF; Investigation: DS, AL, KK, EK; Project administration: DS, EK; Resources: EK; Supervision: EK, AO; Visualization: DS, AL; Writing – original draft: DS; Writing – review & editing: AO, AL, AKF, KK, JS, EK.

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Declarations

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RESEARCH ARTICLE

A network perspective on cognition in individuals with Parkinson's disease

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Abstract

INTRODUCTION: In neuropsychological diagnostics, the assignment of cognitive tests to domains is usually not empirically based. Hence, we aimed to assess the

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dimensionality structure of cognition in individuals with Parkinson's disease (PD) and conceptually replicate the findings in cognitively healthy individuals (CHIs).

METHODS: We performed Exploratory Graph Analysis (EGA) for dimensionality analysis of cognitive test scores in $N = 698$ individuals with PD from the DEM-PARK/LANDSCAPE study. Redundancy was reduced based on Unique Variable Analysis (UVA) before re-performing EGA. CHI data ($N = 60,398$) served as a conceptual replication base.

RESULTS: EGA identified five dimensions. After removing redundancy identified by UVA, EGA identified a unidimensional structure of cognitive test scores. The findings were conceptually replicated in CHIs.

DISCUSSION: The findings imply the need to re-evaluate the composition of cognitive test batteries to reduce redundancy and improve the validity of cognitive diagnostics. Cognition may be better described as a network of interrelated cognitive functions rather than a factorial structure of latent cognitive domains.

KEYWORDS

cognitive decline, cognitive domains, dimensionality analysis, mutualism hypothesis, network analysis, network neuropsychology, Parkinson's disease

Highlights

- Cognitive test scores of the same paradigm were strongly associated with each other.
- This finding indicates redundancy in the cognitive test battery.
- After removing redundancy, scores were best represented by unidimensional structures.
- The findings in Parkinson's disease were conceptually replicated in healthy controls.
- The results suggest that cognition should be viewed as a complex "network" of interrelated functions.

1 | BACKGROUND

Although the diagnosis of Parkinson's disease (PD) is based primarily on motor symptoms, there is a large number of accompanying non-motor symptoms, often including cognitive impairment.^{1,2} Mild cognitive impairment (MCI), prevalent in 40% of individuals with PD,³ is characterized by cognitive performance below the age-appropriate norm, but with little or no impact on activities of daily living. More severe cognitive impairment significantly impairing an individual's independence in activities of daily living is referred to as PD dementia (PD-D).⁴

Given the high risk of cognitive impairment for individuals with PD and its implications for disease prognosis and therapeutic decisions, its valid and reliable diagnosis is essential. For diagnosing PD-MCI, guidelines by the Movement Disorder Society (MDS) recommend a detailed neuropsychological examination across five cognitive domains (attention and working memory, executive functions, memory, language, and visuospatial functions) with at least two different tests each.⁵ PD-MCI is diagnosed if at least two tests indicate impair-

ment, that is, performance of at least one standard deviation (SD) below the appropriate norms. In addition, the MDS guidelines propose differentiating single-domain (one cognitive domain impaired) and multiple-domain PD-MCI (two or more cognitive domains impaired)⁵ as well as amnesic (if memory is affected) and non-amnesic PD-MCI. With combining of these classifications, we can differentiate four PD-MCI subtypes based on cognitive domains,⁵ which were found to be associated with different prognoses regarding further cognitive decline.⁶

Although cognitive domains play a crucial role in the MDS guidelines for diagnosing PD-MCI and subtypes, the concept of cognitive domains is not well defined, as both definitions of cognitive domains and the assignment of cognitive functions or tests to cognitive domains differ. The diagnostic criteria for neurocognitive disorder in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM)⁷ define six domains (attention, executive functions, learning and memory, language, visual-perceptive function, and social cognition); however, the MDS guideline suggests testing five domains, neglecting

social cognition. In addition, the two guidelines differ in assignments of cognitive functions to domains; for example, regarding working memory (DSM: executive function; MDS guideline: attention) and verbal fluency (DSM: language; MDS guideline: executive function).^{5,7} It is important to note that neither of the two definitions provides empirical justifications for their choice of categorization, providing no binding guidelines that map specific tests to cognitive functions and/or domains. As a result, assignments of tests to cognitive domains might not correctly reflect the underlying latent functions and challenge comparability between studies, thereby potentially limiting the reliability and validity of cognitive diagnoses and subtype classifications.

Given the heterogeneity of conceptually based assignments of cognitive tests to cognitive domains, data-driven approaches to identify the cognitive domain structure in individuals with PD, like factor analysis (FA) methods, are important to ensure valid cognitive diagnostics. However, previous research has shown limitations of this approach when applied to healthy or mixed samples, because group-specific characteristics might be neglected.⁸ It is notable that existing studies even in homogenous samples of individuals with PD could mostly not confirm previously assumed structures of cognitive domains across a range of different methods and assumed structures; for example, using Exploratory FA⁹ or Confirmatory FA (CFA) to test bi-factor models of cognition.¹⁰ An alternative for FA methods is *exploratory graph analysis* (EGA).¹¹ This advanced form of network analysis allows identification of a dimensionality structure within network models. EGA shows comparable or better performance than widely used FA methods¹² and allows for a network perspective on cognition with the possibility of applying dimensionality analysis within the network. Two studies applied EGA to cognitive test scores of subgroups on the spectrum from groups of individuals with healthy cognition over subjective cognitive decline (SCD) and MCI to Alzheimer's dementia (AD), yielding inconsistent results in small sample sizes.^{13,14} Existing studies that apply EGA to cognitive test scores do not fulfill simulation-based sample size recommendations for EGA.¹² Furthermore, EGA for cognitive test scores has not yet been applied in individuals with PD.

Psychometric network analysis of cognitive test scores is a relatively new field of research termed *network neuropsychology*,¹⁵ enabling us to analyze the complex interplay between cognitive functions operationalized as cognitive test scores. Test scores are represented as nodes in a network model, with edges between the nodes representing conditional associations between them.¹⁶ Network analysis is the underlying principle of many functional magnetic resonance imaging (fMRI) analyses,¹⁷ and it has helped to shift our perspective toward viewing the brain as a highly complex and interconnected system (rather than modular). It seems highly plausible that if the underlying anatomic features are represented as a network in the human brain, behavioral outcomes of assessed cognitive functions would be as well. Consequently, network analysis has been emerging recently as a method to analyze interconnections between cognitive functions as well.¹⁵ Furthermore, this method opens the possibility of discarding the idea of an underlying latent factor structure of cognitive domains, that is, a *general factor* (*g-factor*) of intelligence,¹⁸ to model cognition in favor of a mutualism hypothesis waiving latent factors.¹⁹

RESEARCH IN CONTEXT

1. **Systematic review:** The authors reviewed the empirical literature using common online databases (e.g., PubMed) to identify existing dimensionality analyses of cognitive functioning in Parkinson's disease (PD) as well as guidelines for diagnosing cognitive impairment in PD. The assignments of cognitive tests to cognitive domains for research and clinical applications were widely theoretically driven rather than empirically based, threatening the validity of cognitive diagnoses in PD.
2. **Interpretation:** The identification of a unidimensional structure of cognitive test scores following the removal of redundancy suggests a view of cognition as a complex system of interconnected cognitive functions instead of a factorial structure of latent cognitive domains.
3. **Future directions:** More studies that empirically analyze the structure of cognitive functioning in individuals with PD and other conditions are needed, to ensure the validity of cognitive diagnoses in PD and beyond. Ideally, such studies would apply network analysis methods to adequately reflect the complexity of cognitive functioning.

In this study, we aim to empirically analyze the network and dimensionality structure of cognitive test scores in a sample of individuals with PD from the DEMPARK/LANDSCAPE cohort study²⁰ with EGA. This approach enables us to compare the results to a previously assumed theoretical structure, both qualitatively and quantitatively. Finally, we will critically evaluate the cognitive test battery used and validate our findings in a large sample of cognitively healthy individuals (CHIs) that was compiled in a factor meta-analysis conducted by Agelink van Rentergem et al.²¹

2 | METHODS

2.1 | Participants

We analyzed the baseline data of individuals with PD from the *Dementia and Parkinson's disease/Langzeitbeobachtung dementieller Symptome und cognitiver Parameter sowie Anwendbarkeit neuer prognostischer Marker bei der Parkinson-Erkrankung* (DEMPARK/LANDSCAPE) study,²⁰ a completed, observational, prospective multi-center cohort study that aimed to characterize the natural course of cognitive decline in individuals with PD. Participants were recruited consecutively from nine movement disorder centers across Germany. Inclusion criteria were age between 45 and 80 years and a diagnosis of idiopathic PD based on the UK Parkinson's Disease Society Brain Bank criteria. The study included individuals with cognitive functions within the

TABLE 1 Cognitive tests in the DEMPARK/LANDSCAPE study.

Theoretically assumed cognitive domain	Test score	Abbreviation
Attention	Digit Span forward ³⁰	DSfw
	Brief test of attention ³¹	BTA
	Stroop word reading ³²	StrW
	Stroop color naming ³²	StrC
	Stroop interference ³²	StrI
Executive functions	Semantic Word Fluency ^a	SemWF
	Phonematic Word Fluency ^a	PhoWF
	Trail Making Test B/A ^a	TBA
	Digit Span backwards ³⁰	DSbw
	Modified Wisconsin Card Sorting Test categories ³³	CScat
	Modified Wisconsin Card Sorting Test non-perservative errors ³³	CSnpe
	Modified Wisconsin Card Sorting Test perservative errors ³³	CSppe
Memory	Figures recall ^a	FigR
	Verbal Learning ^a	VbL
	Verbal Recall ^a	VbR
Language	Boston Naming Test ^a	BNT
Visuospatial functions	Figures copying ^a	FigC
	Leistungsprüfsystem 7 ³⁴	LPS7
	Leistungsprüfsystem 9 ³⁴	LPS9

^aPart of the extended Consortium to Establish a Registry for Alzheimer's Disease (CERAD) neuropsychological test battery (CERAD+).³⁵

demographically adjusted norms (PD-NC), with PD-MCI, as well as with PD-D, following diagnostic criteria for cognitive impairment^{22,23} available at the time of study set-up. Of the original sample ($N = 711$), we excluded those without cognitive classification at baseline (e.g., due to missing data) or whose data for the cognitive variables of interest were completely missing. The final sample for data analysis consisted of $N = 698$ individuals with PD.

2.2 | Cognitive and clinical assessment

An overview of the cognitive test battery and the corresponding theoretically assigned cognitive domains in the DEMPARK/LANDSCAPE study²⁴ are reported in Table 1. Domain assignment was based on experts' opinions. Raw cognitive test scores were demographically adjusted and standardized using published normative data (e.g., to percentiles, z-scores, or *T*-scores). Subsequently, these standardized scores were uniformly transformed into z-scores. For descriptive statistics and distributions of cognitive test scores, see Figure S1. In addition, the data include sociodemographic variables (age, gender, years of education), clinical variables (disease duration; levodopa equivalent daily dose [LEDD]; Unified Parkinson's Disease Rating Scale Part III [UPDRS-III]²⁵; Hoehn & Yahr stages²⁶; Geriatric Depression Scale [GDS²⁷]), and variables for the global cognitive status (Mini-Mental State Examination [MMSE]²⁸; Parkinson Neuropsychometric Dementia Assessment [PANDA]²⁹; cogni-

tive status). All assessments were performed during ON medication state.

2.3 | Statistical analysis

Statistical analyses and data visualization were conducted in R.³⁶ We provide the code used for the statistical analyses as [Supporting Information](#). First, to test if the cognitive test data are suitable for estimating a network model, we applied the Loadings Comparison Test (LCT³⁷), an algorithm based on neural networks that was trained to predict if data were generated from a latent factor model or a network model.

For dimensionality analysis, we applied EGA¹¹ with the Louvain algorithm. EGA constitutes an expansion of the correlation matrix as a unidimensionality method³⁸ to a glasso-regularized gaussian graphical model (*tuning* = 0.5), using R package EGAnet.³⁹ Further details including the code used for data analysis can be found as Supplementary Material. We then applied bootstrapping methods implemented within EGAnet (*bootEGA*, $N = 5000$ boots) to assess stability of the dimensionality analysis. To compare the EGA-derived empirical dimensionality structure with the theoretically assumed domain structure in the DEMPARK/LANDSCAPE study,²⁴ we computed the Total Entropy Fit Index (TEFI⁴⁰) as well as model fit indices Chi², Comparative Fit Index (CFI), and Root Mean Square Error of Approximation (RMSEA) based on CFA.

Following, as recommended to be used with EGA,⁴¹ we performed Unique Variable Analysis (UVA⁴²) to identify possible redundancies in

the test battery. UVA computes the *weighted topological overlap* (wTO), which “quantifies the extent to which a pair of nodes have (dis)similar connections”.^{42,43} Variable pairs identified with wTO >0.25 indicated substantial redundancy⁴²; thus we removed all but one variable from a set of redundant variables. Specifically, the variable showing the lowest maximum wTO with all other variables other than the one with which it is redundant is retained, whereas the other is removed.⁴² Finally, we re-analyzed the now-reduced set of cognitive test data applying EGA as described above.

2.4 | Exploratory conceptual replication of findings in a sample of CHI

For an exploratory conceptual replication of our findings of EGA and UVA in the sample of individuals with PD from the DEM-PARK/LANDSCAPE study, we used publicly available data of a large sample of CHIs compiled by Agelink van Rentergem et al.¹⁷ Following a systematic literature search, they performed a factor meta-analysis with cognitive test data of $N = 60,398$ CHIs from 55 studies. All studies were published after 1997, and administered cognitive tests in a population of CHIs (i.e., without psychiatric or neurological disorders, disorders that could interfere with test administration, and conditions that were studied for their cognitive implications) without any further manipulations. The authors identified an overlap of 12 cognitive tests between the studies that were used for analysis (see Table S1). For this study, we used the total partial correlation matrix of the test variables that eliminated the influence of age, gender, and education from the data, as reported by Agelink van Rentergem et al.²¹ Based on this matrix, we applied EGA with the same configurations as in the analysis of individuals with PD from the DEM-PARK/LANDSCAPE study. We then again performed UVA to identify and remove possible redundancy in the data and re-performed EGA with reduced data.

3 | RESULTS

3.1 | Sample characteristics

In our sample of individuals with PD from the LANDSCAPE/DEMPARK baseline ($N = 698$), participants were $M = 67.62$ years old ($SD = 7.99$), 67.48% were male, and 32.52% were female. The sample included $n = 282$ individuals with PD-NC, $n = 314$ individuals with PD-MCI, and $n = 102$ individuals with PD-D. For further information on the descriptive sample characteristics of sociodemographic, clinical, and cognitive variables, see Table 2.

3.2 | EGA of cognitive test scores in PD

LCT predicted that the cognitive test data from the DEM-PARK/LANDSCAPE study was generated from a network model rather than from a latent factor model, with 91.4% of bootstrapped replicate samples suggesting network models.

TABLE 2 Descriptive sample characteristics.

	Individuals with PD $N = 698$
Age, years, mean (SD)	67.62 (7.88)
Gender, n (%)	
Male	471 (67.48%)
Female	227 (32.52%)
Years of education, mean (SD)	13.30 (3.18)
Disease duration in years, mean (SD)	6.78 (5.41)
Levodopa equivalent daily dose, mean (SD)	772.73 (553.31)
UPDRS-III, mean (SD)	23.05 (12.28)
Hoehn & Yahr stages, n (%)	
1	102 (14.61%)
2	337 (48.28%)
3	198 (28.37%)
4	47 (6.73%)
5	10 (1.43%)
Unknown	4 (0.57%)
GDS, mean (SD)	3.48 (3.08)
MMSE, mean (SD)	27.89 (2.24)
PANDA, mean (SD)	21.45 (6.04)
Cognitive status, n (%)	
PD-NC	282 (40.40%)
PD-MCI	314 (44.99%)
PD-D	102 (14.61%)

Note: Data are mean (SD) or n (%) as appropriate.

Abbreviations: GDS, Geriatric Depression Scale; MMSE, Mini-Mental State Examination; PANDA, Parkinson Neuropsychometric Dementia Assessment; PD-D, Parkinson's Disease dementia; PD-MCI, Parkinson's Disease mild cognitive impairment; PD-MCI, Parkinson's Disease normal cognition; UPDRS-III, Unified Parkinson's Disease Rating Scale Part III.

EGA identified five distinct dimensions that differed from the formerly theoretically assumed cognitive domain structure (Figure 1A). The result was confirmed by bootEGA in 64.92% of bootstrapped samples (see Figures S2 and S3 and Tables S2–S6 for network and dimensionality analysis stability results). Visual inspection of the estimated network model and the dimensionality analysis revealed that cognitive test scores originating from the same higher-level test paradigm (e.g., Modified Wisconsin Card Sorting Test [MWCST]; Stroop test; Leistungsprüfsystem) were more strongly related to each other than to other tests/paradigms in the network. Dimensionality analysis did not separate scores from the same higher-level test paradigm in any case, not even if those variables had been conceptually assumed to reflect different cognitive domains, namely Digit Span forward (attention) and Digit Span backwards (executive functions) or Figures Copying (visuospatial functions) and Figures Recall (memory).

Model fit indices of the empirical EGA-derived structure and the theoretically assumed structure of cognitive domains are presented in Table 3.

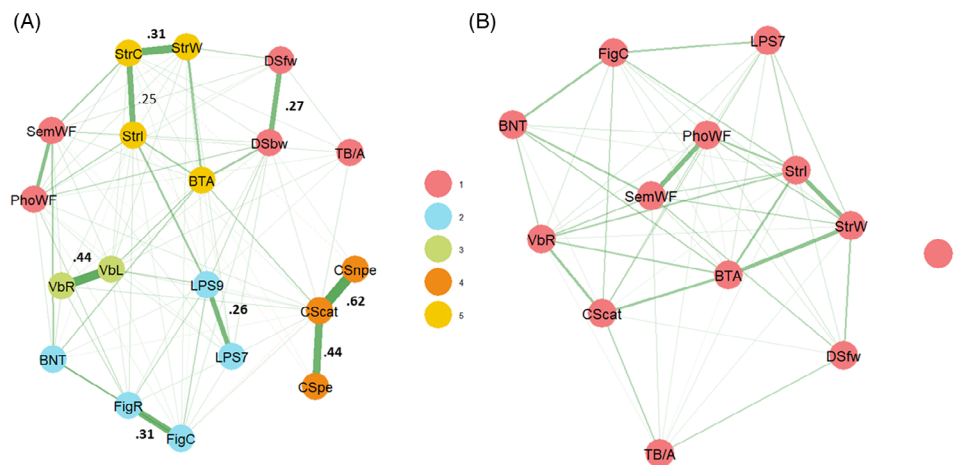


FIGURE 1 Network and dimensionality structure of cognitive functioning in individuals with PD (A) before and (B) after UVA. Green (solid) edges indicate positive pairwise conditional associations; red (dashed) edges indicate negative conditional associations. Node colors indicate assignment to dimensions as empirically derived by EGA. Values near edges indicate wTO, with wTO >0.20 indicating small-to-moderate redundancy, wTO >0.25 indicating moderate-to-large redundancy, and wTO >0.30 indicating large-to-very-large redundancy. Values marked in bold indicate wTO is larger than the cutoff of wTO >0.25 for removal of redundant variables. BNT, Boston Naming Test; BTA, Brief Test of Attention; CScat, Modified Wisconsin Card Sorting Test categories; CSnpe, Modified Wisconsin Card Sorting Test non-perservative errors; CSpe, Modified Wisconsin Card Sorting Test perservative errors; DSbw, Digit Span backwards; DSfw, Digit Span forward; EGA, exploratory graph analysis; FigC, Figures Copying; FigR, Figures Recall; LPS7, Leistungsprüfsystem 7; LPS9, Leistungsprüfsystem 9; PhoWF, phonematic Word Fluency; SemWF, semantic Word Fluency; StrC, Stroop color naming; StrI, Stroop interference; StrW, Stroop word reading; TB/A, Trail Making Test B/A; UVA, unique variable analysis; VbL, Verbal Learning; VbR, Verbal Recall; wTO, weighted topological overlap.

TABLE 3 Model fit indices for empirical and theoretical structures.

Model	Model fit index			
	TEFI	Chi ²	CFI	RMSEA
EGA	−9.54	526.98 (<i>satisfactory</i>)	0.92 (<i>satisfactory</i>)	0.06 (<i>poor</i>)
Theoretical	−7.86	896.72 (<i>satisfactory</i>)	0.78 (<i>poor</i>)	0.10 (<i>poor</i>)

Note: Interpretation in parentheses under values according to Byrne (1994).⁴⁴ Lower TEFI values indicate better model fit. EGA = Structure derived from Exploratory Graph Analysis of cognitive test data of individuals with PD. Theoretical = Previously assumed structure of cognitive tests.²⁴ Abbreviations: CFI, Comparative Fit Index; PD, Parkinson's disease; RMSEA, Root Mean Square Error of Approximation; TEFI, Total Entropy Fit Index.

3.3 | UVA and re-analysis

UVA revealed relevant topological overlap for several pairs of cognitive test scores (Figure 1A). To reduce redundancy within the pool of test scores, test scores for Verbal Learning, Figures Recall, MWCST perseverative errors and non-perseverative errors, Stroop color naming, Leistungsprüfsystem 9, and Digit Span backwards were removed. EGA of reduced data suggested a unidimensional structure (Figure 1B).

3.4 | Exploratory conceptual replication of findings in a sample of CHIs

EGA of cognitive test data in a group of CHIs identified five distinct dimensions (Figure 2A). The result was confirmed by bootEGA in 100% of bootstrapped samples (see Figure S4 and Table S7). Similar to the results from individuals with PD, test scores from the same higher-

level test paradigm were always categorized into the same dimensions. UVA revealed substantial redundancy within several pairs of cognitive test scores from the same higher-level test paradigm (Figure 2A). After removal of the redundant variables Trail Making Test part A, Story Recall direct recall, Digit Span backwards, and Auditory Verbal Learning Test delayed recall, the EGA identified a unidimensional structure (Figure 2B).

4 | DISCUSSION

In this study we analyzed the dimensionality structure of cognitive test scores in a large sample of individuals with PD from the DEM-PARK/LANDSCAPE study with EGA, and compared the results to a theoretically assumed structure of cognitive domains. EGA identified five dimensions in a network model of cognitive test scores, which differed from the theoretically assumed cognitive domain

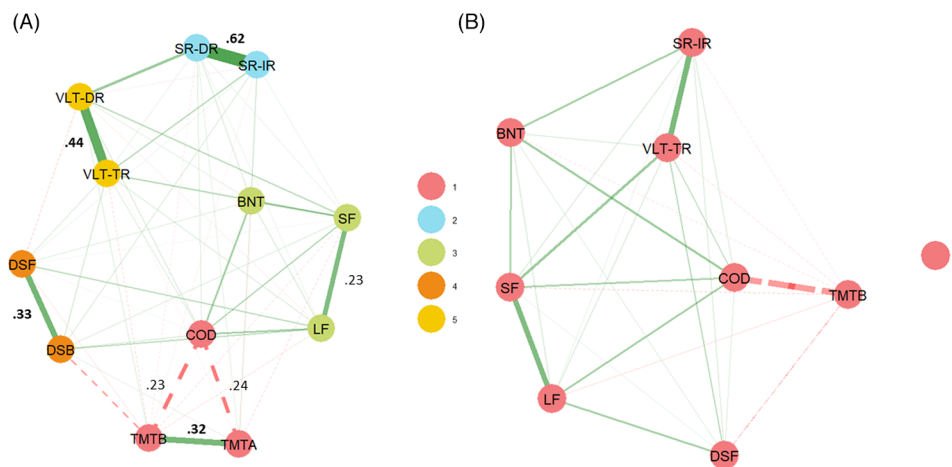


FIGURE 2 Network and dimensionality structure of cognitive functioning in CHIs (A) before and (B) after UVA. Green (solid) edges indicate positive pairwise conditional associations; red (dashed) edges indicate negative conditional associations. Node colors indicate assignment to dimensions as empirically derived by EGA. Values near edges indicate wTO, with wTO >0.20 indicating small-to-moderate redundancy, wTO >0.25 indicating moderate-to-large redundancy, and wTO >0.30 indicating large-to-very-large redundancy. Values marked in bold indicate a wTO larger than the cutoff of wTO >0.25 for removal of redundant variables. BNT, Boston Naming Test; CHIs, cognitively healthy individuals; COD, Coding; DSB, Digit Span backwards; DSF, Digit Span forward; EGA, exploratory graph analysis; LF, Letter fluency; SF, Semantic Fluency; SR-DR, Story Recall direct recall; SR-IR, Story Recall immediate recall; TMTA, Trail Making Test part A; TMTB, Trail Making Test part B; UVA, unique variable analysis; VLT-DR, Auditory Verbal Learning Test delayed recall; VLT-TR, Auditory Verbal Learning Test total recall; wTO, weighted topological overlap.

structure. Specifically, EGA revealed close alignment of higher-level test paradigms with empirically identified dimensions. Further analysis of the EGA-derived structure revealed substantial overlap between test scores from the same higher-level test paradigms, indicating a redundancy of single test scores within the cognitive test battery of the DEMPARK/LANDSCAPE study. Following data reduction, re-performing EGA yielded a unidimensional structure. In an external validation based on a large CHI sample, we successfully conceptually replicated these findings.

Results showed that EGA-derived dimensions were closely aligned with higher-level test paradigms, indicating that these scores are even more closely associated with each other than test scores that were theoretically assigned to the same domain. Thus, for dimensionality analysis, originating from the same paradigm seems to be more influential than the theoretically assumed underlying cognitive domain. This finding aligns with the concept of method variance, which describes the tendency that variables from the same test correlate because their responses are elicited by the same stimuli or methodology.^{8,45} It thus highlights the MDS guideline recommendation of not using two very similar test scores to evaluate cognitive performance within one cognitive domain.⁵ However, our results encourage expanding this recommendation even across theoretically assigned cognitive domains. As an example, test scores Figures Copying (FigC) and Figures Recall (FigR) are theoretically assumed to measure different cognitive domains (visuospatial functions and memory, respectively), but showed substantial overlap in UVA. As a practical implication, an individual presenting impairment in FigC due to impaired visuospatial functions would be likely to show impaired performance in FigR as well, mainly due to a large overlap of the general psychomotor abilities needed for successfully executing the task rather than additional

memory deficits. Nevertheless, this individual would be diagnosed with multiple-domain amnesic cognitive impairment according to standard diagnostic criteria. Hence, our results hint toward a possible inflation of multiple-domain PD-MCI diagnoses and, ultimately, limited validity of the PD-MCI subtypes.

After removing redundant cognitive test scores identified by UVA, re-analyzing the reduced data revealed a unidimensional structure, contradicting both the initially EGA-derived empirical structure and the theoretically assumed structure of cognitive domains. This result might suggest that the concept of cognitive domains is reinforced by strong correlations between redundant test scores due to method variance, creating misleading microfactors.⁴² The unidimensional structure identified by UVA and EGA is in line with two common hypotheses on the structure of cognitive functions: the mutualism hypothesis of intelligence as well as the g-factor hypothesis. The mutualism hypothesis explains positive intercorrelations between cognitive functions by reciprocal associations between cognitive process,¹⁹ not requiring a latent factor like the g-factor.¹⁸ The LCT results of this study support the application of network perspectives of model cognitive functioning compared to a latent factor structure. It highlights network analysis and EGA as appropriate methods and suggests interpretation of our findings as evidence for the mutualism hypothesis rather than the g-factor, although it remains compatible with both. Correspondingly, another study comparing psychometric network models with traditional FA cautiously interpreted their results in favor of the mutualism hypothesis.⁴⁶

Even though this study is one of the first to use EGA to evaluate cognitive tests and, to the best of our knowledge, the first one to use it in a sample of individuals with PD, our findings are unlikely to be an artifact of the EGA method. That is because similar results have been observed

in studies using traditional FA methods. First, a study that performed principal components FA to cognitive test data of individuals with PD-MCI showed method variance as well, even if they were theoretically assumed to represent different cognitive domains: for example, Digit Span forward and Digit Span backwards.⁴⁷ Second, in the factor meta-analysis with cognitive test data of CHIs by van Rentergem et al.,¹⁷ the best fitting model consistently grouped test scores from the same test paradigm into the same factor too.

A limitation of this study is that our sample consisted of individuals with different cognitive statuses (PD-NC, PD-MCI, PD-D). As it has been shown that different clinical groups show specific organizations of cognitive functions,⁸ this might be true for cognitive state subgroups within the same clinical group as well. Network neuropsychology studies have shown that cognitive organization can change with the onset of cognitive impairment, being reflected in network characteristics like node strength centrality.^{14,48} Existing network neuropsychology studies aiming to identify communities within network models were heterogeneous regarding statistical method, sample size, group of interest, and cognitive test scores included.¹⁵ Two studies applying EGA showed that the number of dimensions identified changed on the spectrum from groups of individuals with healthy cognition over SCD and MCI to AD.^{13,14} However, results showed no consistent trend of an increasing or decreasing number of dimensions across this spectrum. These findings may be limited in generalizability and robustness, as they by far did not reach the recommended sample size of $n = 500$ to apply EGA for each group.¹² To comply with this simulation-based recommendation for sample size, we decided not to split the sample into subgroups of different cognitive statuses. Future studies should focus not only on cross-sectional network and dimensionality analysis, but also on longitudinal approaches, for example, by applying dynamical EGA,⁴⁹ which can perform longitudinal dimensionality analysis based on network models. This could help to gain a deeper understanding of how the organization of cognitive functioning may change over time.

Another limitation to consider is the exploratory and data-driven approach applied in this study. Although it is possible to establish the stability of network analysis and EGA results by applying bootstrapping methods, it is not possible, to date, to establish the stability of UVA results. Hence, specific findings based on the UVA algorithm, for example, the degree of redundancy of specific variable pairs, need to be interpreted with caution. However, by conceptually replicating our findings in a different dataset with a different cognitive test battery, we provided evidence for the stability of the overarching finding that redundancy within cognitive test batteries could bias the empirical analysis of the cognitive functioning structure.

It is important to note that we also do not believe that our EGA results should be interpreted as the true structure of cognitive functions, as cognitive test scores do not necessarily reflect isolated cognitive functions. Thus, our findings might reflect a measurement problem regarding cognitive functions in general. Therefore, this issue is not limited to the network neuropsychology framework, but is also relevant to traditional FA methods. Furthermore, we would argue that criteria for cognitive diagnostics relying on cognitive test scores should

consider the test score structure rather than a theoretical structure of cognitive functions. Hence, applying EGA, especially in combination with UVA, can be a useful tool for retrospectively evaluating the validity of cognitive test batteries. We believe that our retrospective analysis can influence future test battery compositions to improve valid and reliable measurement, reduce redundancy, and ensure the validity of cognitive diagnoses and their subtypes as we know them. Simultaneously, it also may pave the way for challenging the concept of cognitive domains and the diagnosis criteria that are associated with them in favor of concepts that reflect the complexity of cognition as an interconnected system. However, future research will need to develop appropriate test batteries, convenient parameters to evaluate cognitive performances, and adequate criteria for diagnosing cognitive impairment within this framework, which do not yet exist.

A strength of this study is that it is one of the first to systematically evaluate the structure of cognitive domains while taking a network perspective on cognition, especially in the groups of individuals with PD (and CHIs). Taking the first step to fill the gap in this under-investigated field, we applied an exploratory dimensionality analysis approach and integrated confirmatory approaches by comparing two empirically derived structure with a prior theoretically assumed structure using CFA. Future studies aiming to replicate our findings should ideally be preregistered with clear hypotheses to further improve confidence in these findings.

We believe that one major strength of this study is combining network and dimensionality analysis by applying EGA. As we already mentioned, theoretical¹⁹ as well as empirical aspects (results of the LCT) support the view of cognition as a complex network of interacting cognitive functions. To make inferences about complex interconnected systems like cognition, we need to apply methods that can adequately reflect this complexity, like network analysis methods.¹⁶ Another strength is that we were able to conceptually replicate our findings in another, independent, large sample of CHIs,²¹ providing first evidence that our results are conceptually replicable and generalizable, and not specific to PD. Furthermore, analyses were based on demographically adjusted, standardized z-scores in the PD sample and by partial correlation in the CHI sample. Even though demographical adjustments differed between cognitive test scores, there were no hints that results were biased by the influences of demographical variables.

5 | CONCLUSION

To conclude, by combining network and dimensionality analysis by applying EGA to cognitive test scores of almost 700 individuals with PD, we found that theoretically assumed categorizations of cognitive test scores into cognitive domains could not be replicated. Furthermore, results showed a high redundancy between test scores, having profound implications for the validity of PD-MCI diagnoses and subtype classifications, as well as the composition of cognitive test batteries in this context. Conceptually replicating the results in a large sample of CHIs, we interpret our findings in the light of the emerging field of network neuropsychology, arguing that cognitive functioning can be

viewed as a complex network of interconnected cognitive functions rather than a latent factor structure with modular cognitive domains.

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CONFLICT OF INTEREST STATEMENT

D.S., M.B.G., D.B., R.H.R., B.M., K.R., O.R., S.R., J.B.S., A.S., C.T., H.U.W., R.D., and A.O. have no competing interests to declare. E.K. received grants from the German Ministry of Education and Research, the Joint Federal Committee, and The German Parkinson Foundation, all outside the submitted work. E.K. received honoraria from the companies EISAI GmbH, Germany, memodio GmbH, Germany, Desitin GmbH, Germany, and Prolog GmbH, Germany, all outside the submitted work. J.K. is a consultant and speaker for AbbVie, Bial, Biogen, Desitin, Esteve, Novartis, Roche, STADA, UCB Pharma, and Zambon; in addition, he is Specialty Chief Editor for *Frontiers in Neurology* (section Applied Neuroimaging) and Associate Editor (Neurology) for *Therapeutic Advances in Chronic Disease*. I.L.S. reports funding from Bayer AG and travel grants from Desitin and the German Society for Neurology outside the submitted work. K.W. receives funding from the Deutsche Forschungsgemeinschaft (German Research Association) and STADAPHARM GmbH outside the present study. He has received honoraria for presentations/advisory boards/consultations from BIAL, Indorsia, Boston Scientific and STADAPHARM GmbH, outside the present study. He has received royalties from Thieme Press and Elsevier Press. He serves as an editorial board member of Wiley's *Parkinson's Disease*, *Behavioural Neurology*, and *PLOS One*. Author disclosures are available in the [Supporting Information](#).

CONSENT STATEMENT

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All study procedures of the DEMPARK/LANDSCAPE project were approved by the Ethics Committee of Philipps University Marburg (approval-no. 178/07) in March 2009, and thereupon by the ethics committees of the participating centers. All participants gave written informed consent prior to their inclusion in the study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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Temporal dynamics of cognitive functioning in people with Parkinson's disease



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Cognitive domains are central to diagnosing cognitive impairment in people with Parkinson's disease (PwPD), yet are defined by expert consensus and cross-sectional data that assume temporal stability. This study examined whether cognitive domains remain stable or reorganize dynamically over time in PwPD. Using dynamic exploratory graph analysis, we analyzed 19 cognitive test scores from 355 PwPD across four yearly assessments (24,372 data points) from the DEMPARK/LANDSCAPE-study to identify dynamic organization of cognitive dimensions. Panel graphical vector autoregression models assessed dynamic couplings among dimensions. Five dynamic cognitive dimensions emerged, diverging substantially from theoretical domains and cross-sectional dimensions at baseline. Dynamic coupling revealed a temporal separation between card-sorting/cognitive flexibility and visuoconstruction. Cognitive domains in PwPD reorganize over time rather than remaining stable, challenging the static assumption of diagnostic criteria. Using PD as an exemplar, findings demonstrate the need for dynamic frameworks potentially revealing condition-specific temporal architectures when applied to other neurodegenerative disorders.

Understanding subtypes of cognitive impairment, i.e., single- or multiple domain mild cognitive impairment (MCI)¹, is crucial for predicting further cognitive decline² or to inform individualized cognitive interventions in neurodegenerative diseases such as Parkinson's disease (PD)³. However, existing definitions of cognitive domains in different guidelines of cognitive diagnostics, e.g., the Movement Disorder Society (MDS) diagnostic

guidelines for PD-MCI¹ or the Diagnostic and Statistical Manual (DSM)⁴ diagnostic criteria for neurocognitive disorder, are mainly based on expert consensus rather than empirical findings. Remarkably, a recent scoping review on empirical findings in people with PD (PwPD) do not support either of those cognitive domain definitions which differ in how specific cognitive tests are assigned to cognitive domains⁵. This discordance

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exemplifies a broader challenge in neurodegenerative disorder diagnostics: the lack of empirically-derived, temporally-validated cognitive domain structures.

Existing empirical domain definitions of cognitive domains in PwPD rely almost exclusively on cross-sectional dimensionality reduction techniques such as factor analysis, which identify how cognitive test scores cluster at a single time point⁷. However, such static analyses may not accurately capture the temporal dynamics of cognitive change within and between cognitive domains. Longitudinal associations between cognitive test scores can diverge from cross-sectional patterns due to statistical phenomena such as Simpson's paradox⁶, where group-level trends can obscure or reverse within-subject changes over time. Misinterpreting these dynamics risks undermining diagnostic accuracy and prognostic precision. Thus, understanding the longitudinal interplay between cognitive test scores is critical for refining diagnostic classifications and ensuring valid and reliable cognitive diagnostics in PD and other conditions. In addition, we can only reliably identify mechanisms of cognitive decline by linking cognitive-behavioral data with potentially relevant diagnostic and prognostic biomarkers, such as neuroimaging measures, genetic factors, or digital biomarkers, when based on valid and reliable cognitive diagnostics.

Understanding cognitive decline in neurodegeneration requires moving beyond static descriptions to examine temporal dynamics at two levels. First, we must identify the dynamic organization of cognition - how individual cognitive tests cluster together *over time* rather than at single timepoints, which may reveal fundamentally different structures. Second, we must characterize dynamic coupling between dimensions - how changes in one cognitive process accelerate, buffer, or reorganize changes in others. While previous longitudinal studies have explored cognitive trajectories in PD by focusing on predicting conversion to PD-MCI or PD dementia (PDD)⁷⁻⁹ or independent domain-specific declines¹⁰, few studies have examined how cognitive domains dynamically interact with one another longitudinally. Emerging network approaches such as panel graphical vector autoregression (GVAR) models¹¹ enable direct examination of these temporal dependencies between cognitive dimensions.

This study addresses two research questions using longitudinal panel data from PwPD across the cognitive spectrum in the DEMPARK/LANDSCAPE study¹². First, we aim to identify dynamic organization of cognitive test scores in PwPD in the DEMPARK/LANDSCAPE study and descriptively compare them to both a theoretically assumed domain structure¹³ and a previously derived empirical, cross-sectional domain structure¹⁴ from the same cohort. To adequately capture the complexity of cognitive functioning, we employ dynamic exploratory graph analysis (dynEGA)¹⁵, which performs a longitudinal clustering based on psychometric network models of cognitive test scores, indicating which test scores show similar changes over time. Second, we seek to characterize dynamic coupling, i.e., dynamics of cognitive change between identified cognitive dimensions to improve our understanding of cognitive decline mechanisms in PD and inform more precise diagnostic and therapeutic strategies. For this, we employ panel vector autoregression (GVAR) models¹¹, enabling us to identify which dimensions predict other dimensions (or themselves) in the next measurement occasion.

Results

Sample descriptives

Our sample of PwPD from the DEMPARK/LANDSCAPE study ($N = 355$) consists of $n = 185$ individuals with Parkinson's disease with cognitive functions within the demographically adjusted norms (normal cognition, PD-NC), $n = 145$ individuals with PD-MCI, and $n = 25$ individuals with PDD at baseline. Participants were $M = 66.22$ years old ($SD = 7.76$), 69.90% were male, and 31.10% were female. Descriptives of the sample characteristics of sociodemographic, clinical, and cognitive variables are provided in Table 1 and Tables S1–2.

Table 1 | Descriptive characteristics of the sample at baseline ($N = 355$)

Variable	Value
Age in years	66.22 (7.76) [45–80]
Gender	
Male	245 (69.90%)
Female	110 (31.10%)
Years of education	13.73 (3.11) [8–20]
Disease duration in months	70.82 (57.27) [0–297]
Levodopa equivalent daily dose	667.37 (446.08) [22.20–2676.60]
UPDRS-III	20.61 (10.44) [1–55]
Hoehn & Yahr stages	
1	69 (19.44%)
2	192 (54.08%)
3	78 (21.97%)
4	14 (3.94%)
unknown	2 (0.56%)
Motor phenotype	
Tremor dominant (TR-D)	35 (9.86%)
akinetic rigid (PIGD-D)	279 (78.59%)
Not determined (ND)	31 (8.73%)
Missing data	10 (2.82E%)
GDS	3.07 (2.79) [0–14]
MMSE	28.34 (1.98) [18–30]
PANDA	22.91 (5.44) [3–30]
Cognitive status	
PD-NC	185 (52.11%)
PD-MCI	145 (40.85%)
PDD	25 (7.04%)

Data are mean (standard deviation) [range] or n (%) as appropriate. MMSE Mini-Mental State Examination (score range 0–30; cut-off for cognitive impairment ≤ 26); PANDA Parkinson Neuropsychometric Dementia Assessment (score range 0.30, cut-off for cognitive impairment ≤ 18); UPDRS-III Unified Parkinson's Disease Rating Scale Part III (score range 0–132; cut-off for moderate motor severity ≥ 33 ; cut-off for severe motor severity ≥ 59); GDS Geriatric Depression Scale (score range 0–15; cut-off for mild depressive symptoms ≥ 6); PD-MCI Parkinson's Disease normal cognition, PD-MCI Parkinson's Disease mild cognitive impairment, PDD Parkinson's Disease dementia.

Dynamic organization of cognitive test scores

We estimated a longitudinal psychometric network model of standardized cognitive test scores, representing how changes in each of the cognitive test scores relate to one another. The derived dimensionality structure indicates which scores showed similar rates of change over the course of four yearly assessments. Five temporally dynamic dimensions of cognitive test scores emerged from dynEGA based on the within-subjects rate of change over time (Fig. 1). Standardized network loadings, similar to factor loadings, for each test are presented in Table S3. The emergent dimensional structure diverged from the theoretically assumed cognitive domains (Table 1) and previously reported cross-sectional factor structures. The adjusted Rand index, a quantitative, descriptive measure for overlap of clustering solutions, indicated a value of 0.41 for the comparison of the dynEGA with the crossEGA structure and 0.21 compared to the theoretically assumed cognitive domain structure. These values indicate moderate agreement with the crossEGA structure and lower agreement with the theoretically assumed cognitive domain structure. In sum, the dynEGA revealed a reorganization of cognitive test scores compared to the static cognitive domain models.

Dimension 1 (*visuoconstruction*) encompasses two interdependent tasks, CERAD + ¹⁶ Figures Copy and Figures Recall. Both require cognitive processes such as spatial reasoning and motor praxis and share identical

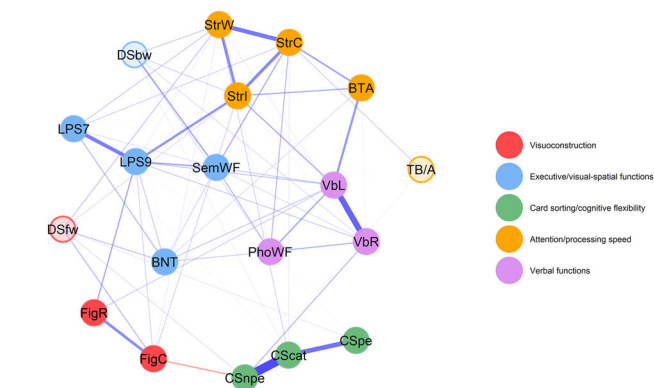


Fig. 1 | Network and dimensionality structure of cognitive test scores from people with Parkinson's disease. Network and dimensionality structure of cognitive test scores from people with Parkinson's disease resulting from dynamic exploratory graph analysis. Blue edges indicate positive pairwise conditional associations; red edges indicate negative conditional associations. Node colors indicate assignment to dimensions as empirically derived by dynamic exploratory graph analysis. Transparent node color indicates network loadings below the cut-off for relevancy (.100). Dimension names were assigned by the authors based on mutual task features of cognitive test scores within dimensions. Abbreviations: BNT Boston Naming Test, BTA Brief Test of Attention, CScat Modified Card Sorting Test categories, CSnpe Modified Card Sorting Test non-perservative errors, CSpe Modified Card Sorting Test perservative errors, DSbw Digit Span backward, DSfw Digit Span forward, FigC Figures Copy, FigR Figures Recall, LPS7 Leistungsprüfungssystem subtest 7, LPS9 Leistungsprüfungssystem subtest 9, PhoWF phonematic Word Fluency, SemWF semantic Word Fluency, StrC Stroop color naming, StrI Stroop interference, StrW Stroop word reading, TB/A Trail Making Test quotient B/A, VbL Verbal Learning, VbR Verbal Recall.

response formats (Tables S4–5). However, CERAD+ Figures Recall depends on stimuli encoded during the Figures Copy task, additionally requiring memory processes. The third task within dimension 1, Digit Span forward¹⁷, often described as a short-term memory task, showed very low network loadings, suggesting low reliability and potentially explaining the weak conceptual alignment with the other tasks.

Dimension 2 (*executive/visual-spatial functions*) consists of two tasks of the German test battery *Leistungsprüfungssystem* (LPS)¹⁸ focusing on spatial rotation (LPS7) and spatial reasoning (LPS9), CERAD+ semantic word fluency, the CERAD+ Boston Naming Test (BNT), and Digit Span backward¹⁷. While most tasks in this dimension involve attentional components, they differ in specific cognitive processes and task features: LPS9 requires more executive processes (e.g., memory updating and planning) than LPS7 (both united by visual stimuli), while these executive processes are also reflected in semantic word fluency. Among others, the BNT requires semantic memory, which is a shared feature with LPS7 and semantic word fluency, and shares stimuli features with both LPS subtests.

Dimension 3 (*card sorting/cognitive flexibility*) consists of the Modified Card Sorting Test¹⁹ subscores, reflecting shared demands on logical reasoning, planning, set-shifting, memory updating, divided attention, and response inhibition.

Dimension 4 (*attention/processing speed*) includes the Stroop test²⁰ subscores, the Brief Test of Attention (BTA)²¹, and the CERAD+ Trail Making Test (TMT) B/A quotient, though the latter showed very low network loadings. Common cognitive processes required are selective and sustained attention, semantic memory, and, partly, response inhibition. The timed response format of the Stroop subscores and the TMT reflect a processing speed component, which also applies to the rapid memory updating required in the BTA.

Dimension 5 (*verbal functions*) consists of the CERAD+ verbal learning and recall tasks alongside CERAD+ phonemic verbal fluency. Mutual cognitive processes required include semantic memory, response inhibition, and, depending on strategy use, vocabulary knowledge.

These tasks also share a similar response types and modalities, suggesting verbal functions as the common component.

In comparison to a previously published cross-sectional EGA model (crossEGA)¹⁵, only the *card sorting/cognitive flexibility* dimension remained stable across both models. All other dynEGA dimensions consist of test scores from two different crossEGA dimensions (Fig. 2), underscoring how cross-sectional structures may mislead the interpretation of the dynamic architecture of cognitive change in PD. In summary, dynEGA results showed different dimensionality patterns than the previously published crossEGA results.

Subsampling stability analyses showed that the dynEGA five-dimension solution could be replicated in 56.7% of subsamples, whereas a four-dimension solution appeared in 42.6%, and three- and six-dimension solution appeared in <1% of the iterations (Table S6). The average silhouette width of 0.69 indicated a good coherence of clustering during subsampling. A sensitivity analysis accounting for systematic effects of sex, age, education, motor impairment, and depression severity resulted in a comparable five-dimensional dynEGA solution. Both the subsampling and sensitivity analysis revealed overall stability of the original dynEGA solution; rather unstable test scores were already flagged with low network loadings (Digit Span forward, Digit Span backward, TMT B/A quotient) or cross-loadings (BTA) in the original dynEGA model. Another sensitivity analysis revealed no study center effects on the dynEGA structure. Detailed results of stability and sensitivity analyses can be found in Figs. S1–3.

When comparing dynEGA dimensions and theoretically assumed cognitive domain structures regarding their predictive utility for clinically relevant outcomes, linear mixed-effects models demonstrated a better model fit for dynEGA dimensions for predicting the Mini Mental State Examination (MMSE) total score (dynEGA: AIC = 3619.54, BIC = 3673.82, LL = -1798.77; theoretically assumed domains: AIC = 3621.87, BIC = 3676.16, LL = -1799.94; Δ AIC = 2.33). Detailed model information are reported in Tables S7–9.

Dynamic coupling of identified cognitive dimensions

We performed panel GVAR analysis to evaluate if one dimension predicts another dimension (or itself) in the next measurement occasion. Panel GVAR analysis revealed dynamic coupling between the cognitive dimensions identified by the dynEGA (Fig. 3), revealing directional dependencies. These patterns suggest temporal ordering in cognitive decline rather than simultaneous deterioration across domains.

The temporal model showed positive autoregressions for dimensions *verbal functions*, *executive/visual-spatial functions*, and *attention/processing speed*: Individuals who perform well (or poorly) in one of these dimensions tend to maintain that relative standing at the next assessment. In contrast, *card sorting/cognitive flexibility* showed a negative autocorrelation, indicating that higher performance at one time point is associated with lower performance at the next assessment (or vice versa). This effect may indicate fluctuations in this dimension's performance, showing as rebound pattern where deviations from an individual's typical level are followed by corrections in the opposite direction.

Cross-dimensional couplings revealed temporal precedence relationships. *Executive/visual-spatial functions* and *attention/processing speed* show bidirectional positive coupling, indicating that performance in one of these dimensions positively predicts performance in the other dimension during subsequent assessment. *Verbal functions* positively predict performance in *executive/visual-spatial functions* in the next assessment. *Card sorting/cognitive flexibility* shows a negatively directed edge towards *visuoconstruction*, indicating that better performance in *card sorting/cognitive flexibility* at one time point is coupled with worse performance in *visuoconstruction* at the next time point.

Sensitivity analysis in those with clinically meaningful cognitive impairment (PD-MCI, PDD) at baseline largely replicated this pattern but revealed two notable differences (see Fig. S4). First, positive coupling between dimensions *visual-spatial functions* and *verbal functions* reversed direction. Specifically, performance in *executive/visual-spatial functions* at

Fig. 2 | Comparison of cognitive domain structures. Cognitive domain structures of cognitive test scores from people with Parkinson's disease resulting from dynamic exploratory graph analysis, theoretical considerations, and cross-sectional exploratory graph analysis. Green edges indicate positive pairwise conditional associations; red edges indicate negative conditional associations. Node colors indicate assignment to dimensions as empirically derived by dynamic exploratory graph analysis. Abbreviations: BNT Boston Naming Test, BTA Brief Test of Attention, crossEGA cross-sectional exploratory graph analysis, CScat Modified Card Sorting Test categories, CSnpe Modified Card Sorting Test non-perseverative errors, CSpe Modified Card Sorting Test perseverative errors, DSbw Digit Span backward, DSfw Digit Span forward, FigC Figures Copy, FigR Figures Recall, LPS7 Leistungsprüfungssystem subtest 7, LPS9 Leistungsprüfungssystem subtest 9, PhoWF phonematic Word Fluency, SemWF semantic Word Fluency, StrC Stroop color naming, StrI Stroop interference, StrW Stroop word reading, TB/A Trail Making Test quotient B/A, VbL Verbal Learning, VbR Verbal Recall.

Dynamic exploratory graph analysis				
Executive/ visual-spatial functions	Visuoconstruction	Verbal functions	Card sorting/ cognitive flexibility	Attention/ processing speed
LPS9	FigC	VbL	CScat	StrC
LPS7	FigR	VbR	CSnpe	StrW
SemWF	DSfw	PhoWF	CSpe	StrI
BNT				BTA
DSbw				TB/A
Theoretically assumed domains				
Language	Visuospatial functions	Memory	Executive function	Attention
BNT	FigC	VbL	CScat	StrC
	LPS7	VbR	CSnpe	StrW
	LPS9	FigR	CSpe	StrI
			TB/A	BTA
			DSbw	DSfw
			SemWF	
			PhoWF	
Cross-sectional exploratory graph analysis				
crossEGA Dim1	crossEGA Dim2	crossEGA Dim3	crossEGA Dim4	crossEGA Dim5
DSfw	FigC	VbL	CScat	StrC
DSbw	FigR	VbR	CSnpe	StrW
SemWF	LPS9		CSpe	StrI
PhoWF	LPS7			BTA
TB/A	BNT			

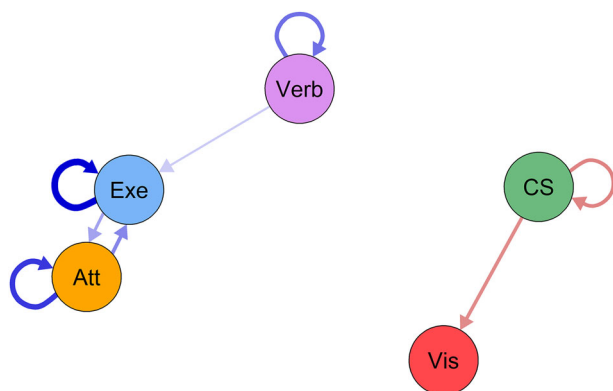


Fig. 3 | Temporal effects network model of cognitive dimensions. Temporal within-subject effect network model of cognitive dimensions derived by dynamic exploratory graph analysis. Blue edges indicate positive pairwise conditional associations; red edges indicate negative conditional associations. Node colors refer to dimensions identified by dynamic exploratory graph analysis as represented in Fig. 1). Abbreviations: Att dimension attention/processing speed, CS dimension card sorting/cognitive flexibility, Exe dimension executive/visual-spatial functions, Verb dimension verbal functions, Vis dimension visuoconstruction.

one time point now predicts performance in *verbal functions* at the next time point of assessment. Second, *attention/processing speed* positively predicts *visuoconstruction*, an association not present in the temporal model of the total sample, potentially indicating that attentional resources become critical for maintaining visuospatial performance only after cognitive resource is depleted.

Discussion

In this study, we assessed the temporal dynamic organization of cognitive dimensions exemplified in PwPD across varied cognitive statuses. We descriptively compared the longitudinal structure to a theoretically assumed cognitive domain structure¹³ and an empirical, cross-sectional cognitive domain structure¹⁴. We found that the longitudinal structure, revealing five cognitive dimensions, diverged substantially from both alternatives.

Cognitive domains might not remain stable over time and static cognitive domain models may misrepresent dynamic cognitive organization. Analysis of dynamic coupling between cognitive dimensions revealed two distinct clusters of temporal effects, indicating domain-wise trade-offs in cognitive performance over time.

Longitudinal dynEGA dimensions, representing associated temporal change between cognitive test scores, i.e., clusters of test scores that showed similar patterns of change over time, differed from both the theoretically assumed cognitive domain structure¹³ and the empirical cross-sectional crossEGA dimensions¹⁴. This difference may be potentially explained by Simpson's paradox, where trends observed at one level of analysis can be reversed when additional explanatory variables are included⁶. While full reversals of the statistical associations are unlikely in this context, the magnitude of associations between cognitive test scores may diminish when focusing on longitudinal within-subject effects rather than cross-sectional between-subject effects. Compared to the cross-sectional dimensions, bias introduced by method variance, i.e., the tendency that test scores correlate with each other because their instructions or stimuli are very similar to each other²², may be reduced in the longitudinal dimensions. While all test scores that are part of the same test paradigm (e.g., CERAD+ Figures Copy and Figures Recall) were consistently categorized into the same cross-sectional dimensions¹⁴, some pairs of test-scores were categorized into different dimensions (e.g., phonemic and semantic word fluency) in the longitudinal dimensions. The adjusted Rand index indicated a moderate overlap of clustering for the comparison of the dynEGA with the crossEGA structure and a lower overlap when compared to the theoretically assumed domain structure. While the adjusted Rand index is a quantitative, descriptive measure, a formal model comparison was not conducted due to cross-sectional versus longitudinal data structures, representing a limitation of the exploratory approach. In sum, differences of identified cognitive dimensions compared to cross-sectional cognitive domain structures may indicate mutual decline of specific cognitive processes required for successfully completing cognitive tasks (Table S4), reflecting a deeper latent structure than cross-sectional task similarity alone.

The dissociation between cross-sectional (static) and longitudinal (dynamic) cognitive organization has important conceptual implications. First, our results challenge the assumption of temporally stable cognitive domains. Rather, they indicate that correlations between cognitive test

scores in cross-sectional data do not necessarily reflect how cognitive processes required in cognitive tasks mutually decline with each other longitudinally. Static cognitive domain models thus may misrepresent dynamic cognitive organization in PwPD – potentially explaining the highly heterogeneous findings of studies aiming to identify a cognitive domain structure from empirical data⁵ – whereas longitudinal clustering identified by dynEGA captures the co-trajectory of cognitive test score change, representing a sequential or staged prorecession of different cognitive functions. Second, our findings highlight the need for consistent and empirically based diagnostic criteria for valid and reliable cognitive subtype diagnostics in both clinical practice and research. Such cognitive subtype diagnoses are not only prognostic for clinical disease progression², but in research are also often linked to potentially relevant diagnostic and prognostic biomarkers, such as neuroimaging measures²³, genetic factors²⁴, or digital biomarkers (e.g., actigraphy data)²⁵. Considering dynamic cognitive organization may increase the validity and reliability of cognitive subtyping based on cognitive domains and, in turn, increase the quality and validity of findings linking cognitive phenotyping to other data modalities for uncovering mechanisms and risk factors of cognitive decline. Our findings showed that longitudinal dynEGA dimensions performed better than the theoretically assumed domains in modeling the MMSE total score as an independent, global cognitive outcome, demonstrating the potential of improving prognostic accuracy of clinically relevant variables. Future studies should expand these findings by evaluating the predictive utility of different cognitive functioning structures for cognitive outcomes and dementia conversion in independent samples. Further, they should investigate the potential predictive utility for other relevant and prognostic biomarkers as described above. Third, our findings may have profound clinical implications. Cognitive screening tests, such as the widely-used MMSE, usually result in a global cognition total score but also rely on clustering of cognitive subitems. A recent study has utilized categorizations of single cognitive screening tasks to cognitive domains in another cognitive screening test, the Montreal Cognitive Assessment, to create proxies for standardized scores of conventional neuropsychological tests²⁶. Showing the increased predictive utility of longitudinal dynEGA dimensions for modeling the MMSE total score suggests that considering temporal information on classifications of cognitive test scores into domains in cognitive screening tests may also help to improve diagnostic accuracy of such screenings tests that are of high clinical relevance for detecting cognitive impairment in PwPD. In addition, cognitive subtyping may be used for planning appropriate personalized cognitive training interventions^{3,27} and could also benefit from taking temporal information about the cognitive reorganization into account. In sum, our findings call into question the reliability and validity of widespread guidelines for cognitive diagnostics based on cognitive domains, such as the MDS guidelines for assessment of PD-MCI¹ or the DSM criteria for neurocognitive disorder⁴.

Similar to factor loadings in factor analyses, it is possible to compute network loadings for dynEGA dimensions¹⁵. Some variables (Digit Span forward, Digit Span backward, TMT quotient B/A) showed very low network loadings, indicating low association of these scores with dynEGA dimensions. Potential reasons might include a generally low reliability of such scores, floor/ceiling effects, or unique longitudinal change patterns that could not be captured by the psychometric network analysis underlying dynEGA, e.g., non-linear trajectories. The TMT quotient already showed very low network loadings in the previously published crossEGA¹⁴, potentially reflecting issues with floor effects resulting from coding failed TMT part B attempts as maximum time. However, visual inspection of the test score distribution (Fig. S5) does not reveal any ceiling/floor effects for our study. Nonetheless, variables with low network loadings should not automatically be discarded as non-informative in clinical practice. For example, Digit Span forward and Digit Span backward showed low network loadings for the dynEGA dimensions, but the highest network loadings for dimension 1 reported in the crossEGA results¹⁴. For cross-sectional purposes of cognitive diagnostics, the Digit Span test scores might still be informative measures to assess cognitive performance in PwPD. Future research should

thus evaluate the significance of network loadings, from both dynEGA and crossEGA, about the informativeness of cognitive test scores and its implications for the compilation of neuropsychological test batteries.

Although we are not aware of existing similar analyses in the context of Alzheimer's disease (AD) or other clinical samples, it seems likely that the described temporal reorganization is a general mechanism and not restricted to cognitive functioning in PwPD. As different clinical samples (e.g., PD vs. AD) show different cross-sectional cognitive profiles²⁸, they might also show differences in their specific configurations of dynamic reorganization. In fact, dynamic reorganizations might be seen as the defining measurable expressions of different (neurodegenerative) disease mechanisms affecting cognition. Thus, future studies should investigate the temporal reorganization of cognitive domains in other clinical samples such as AD.

Panel GVAR analysis revealed dynamic coupling of cognitive dimensions, indicating if one dimension predicts another dimension (or itself) in the next measurement occasion. Notably, *card-sorting/cognitive flexibility* shows a directed negative association towards *visuoconstruction*. This finding aligns remarkably with the dual-syndrome hypothesis of cognitive impairment in PD^{29,30}, which postulates two distinct but overlapping paths of cognitive decline in PD: (1) an early-onset fronto-striatal impairment, manifesting as dopamine-modulated deficits in executive functions and attention, and (2) a later-onset cholinergic-modulated posterior and temporal lobe impairments showing as language (semantic fluency), memory, and visual-spatial dysfunctions, with more rapid decline to PDD. The negative temporal association between *card sorting/cognitive flexibility* and *visuoconstruction* could reflect the separation of early executive deficits of the fronto-striatal path from later visual-spatial deficits of the posterior-cortical path postulated by the dual-syndrome hypothesis³⁰. Importantly, there is no negative association from *card sorting/cognitive flexibility* towards the *executive/visual-spatial dimension*, as the *executive/visual-spatial dimension* seems to reflect both fronto-striatal and posterior-cortical functions, evidenced by (a) the strong attentional and partly executive components when analyzing the underlying cognitive processes, stimuli, and response characteristics (Table S4), and (b) cross-loadings of LPS9 with the *attention/processing speed dimension*. Thus, the *visuoconstruction dimension* seems to reflect the posterior-cortical impairments better than ambiguous visual-spatial tasks additionally relying on executive processes.

Similar to findings of dynamic organization of cognitive domains, dynamic couplings may potentially reflect disease-specific mechanisms and might be related to the dual-syndrome hypothesis of PD. However, without an age-matched control sample, it remains unclear whether the observed temporal dynamics reflect PD-specific processes or general aging-related processes. Future studies should therefore investigate this analytical framework in both healthy and other clinical samples such as AD. In sum, findings of dynamic couplings between cognitive dimensions may be related to theories about the longitudinal development of cognitive functioning in aging or neurodegenerative diseases such as the dual-syndrome hypothesis in PD.

One limitation of the present analyses is that some variables showed potential ceiling effects. However, visual inspection showed distributional shifts decreasing ceiling effects over time (Supplementary Fig. S5), indicating that the longitudinal approach of our analyses could compensate for this potential bias. Further, including all test scores regardless of potential ceiling effects increased comparability with the theoretical cognitive domain structure¹³ and the cross-sectional dimensional structure¹⁴ from the same cohort. In addition, our sample is potentially subject to Berkson's bias, a sampling bias that occurs when sample selection is based on clinical variables that are later included in the analyses³¹. For our analyses, we included data from all participants for whom cognitive test data were available at the fourth time point of the DEMPARK/LANDSCAPE study. Hence, participants who dropped out of the study during the first three time points of assessments due to severe cognitive or motor symptoms are not included in this sample. Consequently, our findings should only be generalized with

caution to the general population of PwPD and especially to the subgroup of PwPD with severe cognitive or motor impairments. To address this potential issue and to focus on mechanisms of cognitive decline, we performed additional GVAR analyses with a subsample of people who already showed cognitive impairment at baseline assessment. Results of these analyses mostly confirmed our findings from the total sample. Further, the majority of our sample showed an akinetic-rigid motor phenotype exhibiting postural instability and gait difficulty (PIGD-D), which has been associated with greater cognitive impairment and decline compared to the tremor dominant (TR-D) and not determined (ND) motor phenotype^{32,33}. Hence, generalizability of the findings to other motor phenotypes may be limited and should be investigated in future studies.

Despite potential confounders including sex, education, depressive symptoms, and motor symptoms, our findings demonstrated overall stability across sensitivity analyses and subsampling procedures. Minor variations in dimensional structure were explained by low network loadings and cross-loadings of specific variables. However, the influence of individual variables on cognitive clustering warrants further investigation, for instance, whether cognitive clustering differs between males and females. Results remained stable when accounting for study center effects in sensitivity analyses. Future studies should also investigate how learning and practice effects, i.e., improvements in mean test scores due to repeated measurement, influence covariance structures, to determine whether and how researchers should account for such effects before applying dynEGA or related techniques.

Further, the effects of therapeutic interventions on the temporal dynamics could not be accounted for in the present analyses due to missingness of this information in the data set. Therefore, temporal dynamics could partly reflect intervention effects rather than intrinsic cognitive organization. First, the levodopa equivalent daily dose (LEDD) was only available for baseline assessment but not for later assessments. Dopaminergic medication could have influenced the underlying covariance matrix as differential effects are reported on various cognitive outcomes. For example, positive effects have been reported on card sorting tasks, task switching or working memory tasks, whereas negative effects have been reported on learning or gambling and decision making²⁹. Due to its mixed and non-linear effects on cognitive functions, identifying, quantifying, and adjusting for medication effects when applying psychometric network analysis such as the dynEGA is complex and requires further investigation. Second, the data set does not contain information on deep brain stimulation (DBS). As DBS was not specified as an exclusion criterion in the DEMPARK/LANDSCAPE study (neither at baseline nor during the course of data collection), some participants may have received DBS before or during the study period. This may have impacted the covariance structure of cognitive test scores due to DBS' differential effects on cognitive functions, including reported negative effects on performance in long-term memory and verbal fluency tasks³⁴. In sum, despite the potential confounders discussed, our findings did not seem to be meaningfully biased or unstable, as indicated by the results of sensitivity analyses and subsampling procedures.

Our results of the GVAR analyses mainly focused on the temporal within-subject network model. However, because yearly measurement intervals may underrepresent measures capturing meaningful short-term changes happening faster than can be represented by first-order derivatives across four consecutive observations, the contemporaneous fixed-effect within-subject network model should be taken into account (Fig. S4A). This model identifies bidirectional predictions between variables within the same measurement occasion after accounting for temporal information, capturing effects occurring faster than the measurement intervals³⁵. The temporal and contemporaneous models show similar patterns, though the contemporaneous model shows an additional positive edge between verbal functions and *card sorting/cognitive flexibility* and does not include the negative edge between *card sorting/cognitive flexibility* and *visuoconstruction*. Future research should incorporate more frequent measurement occasions to better capture short-term cognitive dynamics to reliably estimate longitudinal within-subject network models.

Generalization of our findings is limited by heterogeneity in cognitive test batteries across studies⁵ which may identify different temporal dimensions. For instance, the cognitive assessment battery administered in this study does not fully conform to the recommendations for cognitive assessments in PD-MCI¹ as it includes only one task assessing verbal functions according to the MDS guidelines instead of two. Consequently, both cognitive status classification and the dimensional structure may differ from studies using MDS level II compliant batteries. Importantly, we do not claim to have identified the “true” structure of cognitive domains. Although the longitudinal dynEGA dimensions showed better predictive utility in comparison to the theoretically assumed domains, we do not recommend to simply replace one categorical structure by another. Rather, our findings highlight the importance of empirical studies on cognitive domain organization and the added value of longitudinal approaches to consider dynamic reorganization. Instead, future research should explore new measures of cognitive performance based on the concept of cognition as a complex, interconnected network, moving beyond categorical concepts such as cognitive domains that neglect both temporal dynamics and task-related variances.

The present study shows several strengths. Employing psychometric network analysis allowed us to analyze and visualize cognitive functioning as an interconnected, complex system rather than discrete cognitive domains. Additionally, the longitudinal approach enabled us to identify the temporal dynamics within the network of cognitive functions. Identifying these temporal dynamics may contribute to increase diagnostic accuracy and prognostic precision in cognitive diagnostics by questioning the assumption of temporally stable cognitive domains, possibly initiating refinements in how cognitive tests are assigned to cognitive domains based on longitudinal empirical findings and a stronger focus on specific task features. Another strength is that we were able to descriptively compare various cognitive clustering structures (a theoretical structure¹³, the cross-sectional dimensional structure¹⁴, and the longitudinal dimensional structure) all relying on the same cognitive test battery in the same cohort of PwPD. This increased comparability of these different approaches, which is usually limited by a great variety of the cognitive test scores included in the analyses⁵, and, consequently, validity of the found differences.

To conclude, our findings provide evidence for a dynamic reorganization of cognitive domains in PwPD, challenging the foundational assumption of temporally stable cognitive domains and indicating that static cognitive domain models may misrepresent dynamic cognitive organization. This challenges the validity and reliability of cognitive diagnoses relying on the concept of cognitive domains, such as diagnoses based on the criteria for PD-MCI¹ or neurocognitive disorder⁴. The network perspective on cognitive functioning presents as a useful approach to complement diagnostic guidelines by creating awareness of the interdependence of cognitive test scores and the definitional issues that come with the traditional classification system of cognitive test scores. Identifying the dynamic coupling between cognitive dimensions allows to refine predictions from disease-specific theories of cognitive decline, such as the DSH in PD³⁰ in this study, and to derive new concepts within this framework for other clinical samples. To conclude, our study established a framework for reconceptualizing the (re)organization and temporal coupling of cognitive dimensions.

Methods

Participants

We analyzed longitudinal data from the first four annual assessment time points (i.e., up to the 36-months follow-up) of the DEMPARK/LANDSCAPE study¹², a completed, observational, prospective multi-center cohort study that aimed to characterize the natural course of cognitive decline in PwPD. To ensure appropriate sample size for analyses, we did not include data after the 36-months follow-up. Participants were consecutively recruited from nine movement disorder centers across Germany, entering the study at different time points relative to their diagnosis. Inclusion criteria were age between 45 and 80 years and a diagnosis of idiopathic PD based on

the United Kingdom Parkinson's Disease Society Brain Bank criteria. The total sample included individuals with different cognitive statuses: PwPD with cognitive functions within the demographically adjusted norms (normal cognition; PD-NC), PD-MCI, and PDD. Cognitive diagnoses were based on the diagnostic criteria for cognitive impairment that were available at the time of study set-up^{36,37}. To distinguish PDD from dementia with Lewy bodies, PDD was assumed if parkinsonism preceded dementia by more than 12 months, whereas DLB was assumed if dementia occurred before or concurrently, in accordance with current diagnostic guidelines at the time of recruitment^{12,38}. From the original sample ($N = 711$), we excluded those without available data for the fourth assessment time point ($n = 356$). The final data consisted of 24,372 valid data points (90.3%) across 19 cognitive test scores of $N = 355$ individuals with PD with different cognitive statuses and four time points. Higher proportions of missing data were observed for time points after baseline and for the Modified card sorting items, presumably due to task complexity. Detailed information on missing data is provided in Tables S10–13.

All procedures complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Study procedures of the DEMPARK/LANDSCAPE project were approved by the Ethics Committee of Philipps University Marburg (approval-no. 178/07) in March 2009, and thereupon by the ethics committees of the participating centers. All participants gave written informed consent prior to their inclusion in the study.

Cognitive and clinical assessment

Cognitive functioning was assessed using a comprehensive cognitive test battery administered as part of the DEMPARK/LANDSCAPE study. Table 2 provides an overview of the cognitive tests and their classification into

Table 2 | Cognitive tests and corresponding theoretically assumed cognitive domains in the DEMPARK/LANDSCAPE study

Theoretically assumed cognitive domain	Test score	Abbreviation
Attention	Digit Span forward ¹⁷	DSfw
	Brief Test of Attention ²¹	BTA
	Stroop word reading ²⁰	StrW
	Stroop color naming ²⁰	StrC
	Stroop interference ²⁰	StrI
Executive functions	CERAD+ Semantic Word Fluency ^a	SemWF
	CERAD+ Phonematic Word Fluency ^a	PhoWF
	CERAD+ Trail Making Test B/A ^a	TBA
	Digit Span backwards ¹⁷	DSbw
	Modified Card Sorting Test categories ¹⁹	CScat
	Modified Card Sorting Test non-perservative errors ¹⁹	CSnpe
	Modified Card Sorting Test perservative errors ¹⁹	CSpe
Memory	CERAD+ Figures Recall ^a	FigR
	CERAD+ Verbal Learning ^a	VbL
	CERAD+ Verbal Recall ^a	VbR
Language	CERAD+ Boston Naming Test ^a	BNT
Visual-spatial functions	CERAD+ Figures Copy ^a	FigC
	Leistungsprüfsystem subtest 7 Spatial Rotation ¹⁸	LPS7
	Leistungsprüfsystem subtest 9 Spatial Reasoning ¹⁸	LPS9

^aPart of the extended Consortium to Establish a Registry for Alzheimer's disease neuropsychological test battery (CERAD+) ¹⁶.

theoretically assumed cognitive domains, based on expert consensus¹³. Tables S4–5 provide details on cognitive task features, such as type of cognitive process, stimuli and responses. All neuropsychological assessments were administered in a fixed order. Assessments were administered by various trained examiners both across and within study centers. After standardizing and demographically adjusting the raw cognitive test scores using published normative data to percentiles, z-scores, or T-scores, we uniformly transformed all standardized scores into z-scores. Tables S14–17 and Fig. S5 present descriptive statistics and score distributions for all cognitive test scores. The data also include sociodemographic variables (age, sex, years of education), clinical variables (disease duration; levodopa equivalent daily dose; Unified Parkinson's Disease Rating Scale Part III, UPDRS-III³⁹; Hoehn & Yahr stage⁴⁰; PD motor phenotype; Geriatric Depression Scale, GDS⁴¹), and cognitive variables for the global cognitive status (Mini-Mental State Examination⁴²; Parkinson Neuropsychometric Dementia Assessment⁴³; cognitive status based on clinical evaluation). PD motor phenotypes (tremor-dominant, TR-D; akinetic-rigid exhibiting postural instability and gait difficulty, PIGD-D; not-determined, ND) were based on UPDRS-III scores according to the procedure that was previously reported in other DEMPARK/LANDSCAPE analyses^{32,33}. All assessments were conducted while participants were in the ON medication state.

Statistical analysis

We performed all statistical analyses using R version 4.3.1⁴⁴. We provide the code used for statistical analyses as Supporting Information B.

First, we tested all cognitive test variables on the assumption of stationarity in the data using R package *tseries*⁴⁵. Because the Kwiatkowski-Phillips-Schmidt-Shin (KPSS) test indicated stationarity for all variables except for CERAD+ Verbal Learning ($p = 0.032$), we did not perform any additional measures regarding systematic trends.

To identify dimensions of cognitive test scores that co-evolve longitudinally, addressing our first research question, we applied dynEGA¹⁵ to the full sample across all four timepoints. Unlike traditional factor analysis, which aims to identify cross-sectional latent factors, dynEGA is a clustering method that detects clusters of variables showing associated temporal change within individuals. We applied dynEGA with the Louvain algorithm to a glasso-regularized gaussian graphical model using R package *EGAnet*⁴⁶. The dynEGA used four consecutive observations ($n.embed = 4$) to estimate first-order derivatives ($use.derivates = 1$) of the variables, which can be interpreted as velocity or rate of change over time within individuals⁴⁶. Missing data were handled via pairwise deletion by the dynEGA function, i.e., correlations were computed using all available cases for each variable pair. Dimensions identified by dynEGA represent clusters of cognitive test scores that changed with each other over time within individuals. The Louvain algorithm uses the community clustering method⁴⁷, applying a community detection algorithm repeatedly to the same network and selecting the modal community solution across all iterations ($N = 1000$). We then computed standardized network loadings, which are conceptually analogous to factor loadings, but have different cut-offs for effect size interpretation: values of 0.15 are considered small, 0.25 moderate, and 0.35 large⁴⁸. For a descriptive, quantitative comparison between the dynEGA, the crossEGA, and the theoretically assumed cognitive domain structure, we computed the adjusted Rand index using R package *mclust*⁴⁹. The index quantifies the similarity between cluster solutions by assessing the extent to which variable pairs have been assigned to the same or to different clusters across solutions⁵⁰. Possible values range from -1 to 1 where 1 indicates perfect agreement between clustering solutions, 0 indicates agreement at chance level, and negative values indicate agreement worse than expected by chance.

To assess the stability of the identified dynEGA solution, we performed subsampling procedures with $N = 1000$ iterations and subsamples consisting of 85% of the original sample. Based on the frequencies of variable pairs clustering together, we computed the average silhouette width, which quantifies how stable the groups of variables are that tend to appear together⁵¹. Values above 0.50 are acceptable, values from 0.70 indicate strong

structures with stable clustering⁵¹. To account for potential confounders, we regressed sex, age, years of total education, PD-related motor impairment (UPDRS-III score), and depression severity (GDS score) on each of the cognitive test scores and then calculated the residualized cognitive test scores as the difference between the observed cognitive test scores and the scores predicted by the regression models. We then performed dynEGA on these residualized scores. Another sensitivity analysis accounted for study center effects by linearly regressing a one-hot encoded study center variable on the cognitive test scores.

To compare the predictive utility of dynEGA dimensions versus the theoretically assumed cognitive domain structure, we performed linear mixed-effect models with the MMSE total score as dependent variable, using the *lmer* function of *R* package *lme4*⁵². Predictors were time and (a) the unweighted mean of z-scores of cognitive tests included in each dynEGA dimensions that was computed for each person and time point and (b) the unweighted mean of z-scores of cognitive tests according to the theoretically assumed domains that was computed for each person and time point. Time and the dynEGA dimension mean scores or theoretical cognitive domain mean scores were fixed effects; a random intercept was specified for each individual. We compared the dynEGA model and theoretical cognitive domain model using the Akaike information criterion (AIC), Bayesian information criterion (BIC), and log-likelihood (LL).

To examine how cognitive dimensions are dynamically associated with one another over time, addressing our second research questions, we computed dimension-weighted means for each participant of the total sample based on the network loadings, resulting in five scores per participant, one for each dynEGA dimension. Because dynEGA identifies clusters of cognitive tests that share similar temporal dynamics, these dimension-weighted means can be interpreted as a cognitive dimension composite score reflecting the temporal coherence of tests within dynamic cognitive dimensions. Figure S6 shows descriptive statistics of these scores for each time point. The KPSS test indicated stationarity for all dimension-weighted composite scores used in the analyses. The scores were then used as input for a Graphical Vector Autoregression (GVAR) model using the *R* package *psychonetrics*⁵³. The time variable was defined as the number of months since baseline (0, 12, 24, 36). We report a temporal within-subject network model indicating whether one dimension predicts another dimension (or itself) at the next measurement occasion. This temporal model was pruned ($\alpha = 0.05$) non-recursively using *R*-package *psychonetrics*⁵³, applying the Hochberg correction for multiple corrections. The saturated model is reported in Fig. S7. A contemporaneous within-subject effect network model, indicating if two variables predict one another within the same measurement occasion after taking temporal information into account, and a between-person network model are reported in Fig. S8.

To address a potential selection bias in our study favoring inclusion of PwPD that stay cognitively and bodily healthy over time, interfering with research question two focusing on mechanisms of cognitive decline, we computed another exploratory GVAR model that includes only PwPD already showing cognitive impairment at baseline as sensitivity analysis.

Data availability

The data supporting this study's findings are available on reasonable request from the corresponding author Elke Kalbe in consultation with the DEM-PARK/LANDSCAPE consortium. The data are not publicly available due to privacy and ethical restrictions. The underlying statistical code for this study is available as Supplementary Material B and can be accessed via the online version of the article.

Code availability

The underlying statistical code for this study is available as Supplementary Material B and can be accessed via the online version of the article.

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D.S. — Conceptualization, Formal Analysis, Methodology, Visualization, Writing: Original Draft Preparation. E.K. — Conceptualization, Investigation, Project Administration, Supervision, Resources, Writing: Review & Editing. A.O. — Conceptualization, Supervision, Writing: Review & Editing. M.K.D.: Conceptualization, Methodology, Supervision, Writing: Review & Editing. M.B.G., D.B., R.H.R., J.K., I.L.S., B.M., K.R., O.R., S.R., J.B.S., A.S., C.T., K.W., and R.D. — Investigation, Project Administration, Resources, Writing: Review & Editing.

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Additional information

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